A 46-year-old woman comes to the office due to sexual difficulties for the past year. The patient rarely thinks about sex anymore and frequently declines sex when her husband tries to initiate. She is attracted to her husband and worries that he assumes she is losing interest in him. Although vaginal lubrication is adequate during sex and the patient can reach orgasm, she finds that her mind wanders during the experience. She is unsure what is causing a decrease in her sex drive, although she notes that she received a promotion 3 months ago and has been working longer hours since then. The patient describes her marriage as stable and loving. She has a history of a depressive episode and currently takes bupropion. Physical examination and laboratory studies, including thyroid function tests, show no abnormalities. Which of the following is the most likely diagnosis?

- A. Adjustment disorder
- B. Antidepressant-induced sexual dysfunction
- C. Female orgasmic disorder
- D. Female sexual interest/arousal disorder
- E. Genito-pelvic pain/penetration disorder
- F. Normal menopausal changes

Submit

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- A. Adjustment disorder (23%)
- B. Antidepressant-induced sexual dysfunction (10%)
- C. Female orgasmic disorder (1%)
- ✓ D. Female sexual interest/arousal disorder (49%)
- E. Genito-pelvic pain/penetration disorder (0%)
- F. Normal menopausal changes (15%)

Omitted
Correct answer
D

49%
Answered correctly

02 mins, 21 secs
Time Spent

07/02/2020
Last Updated

Explanation

This patient's lack of sexual desire is most consistent with **female sexual interest/arousal disorder**, a sexual disorder characterized by lack of, or

Explanation

This patient's lack of sexual desire is most consistent with **female sexual interest/arousal disorder**, a sexual disorder characterized by lack of, or significantly reduced, sexual interest and/or arousal. Diagnosis requires ruling out psychological, medical, and substance/medication-related causes of sexual dysfunction (eg, depression, diabetes, chronic alcohol or drug use) and relationship problems.

The diagnosis of female sexual interest/arousal disorder encompasses symptoms of **decreased interest, decreased arousal, or both**. This patient primarily experiences decreased interest (ie, lack of sexual thoughts; reduced initiation of sexual activity or receptivity to a partner's attempts to initiate, but adequate lubrication/orgasm). Symptoms related to arousal may include decreased excitement/pleasure in response to mental and physical sexual cues and encounters.

(Choice A) Although the patient mentions that her condition is worse since her promotion 3 months ago, there is evidence of a change in sexual functioning preceding this stressful event.

(Choice B) Serotonergic antidepressants (eg, selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors) are a common cause of medication-induced sexual dysfunction and can cause decreased libido as well as anorgasmia in women. This patient, however, is taking bupropion, a norepinephrine-dopamine reuptake inhibitor that does not affect serotonin and is unlikely to cause sexual side effects.

(Choice C) Female orgasmic disorder is characterized by marked delay in, decreased frequency and intensity of, or absence of orgasms.

(Choice E) Genitopelvic pain/penetration disorder involves recurrent difficulties with pain or fear of pain with vaginal intercourse or penetration attempts.

(Choice F) Although declining levels of estrogen in peri- and post-menopausal women may be associated with decreased sexual interest in some patients, this is typically accompanied by decreased vaginal lubrication, which this woman does not describe.

Educational objective:
Female sexual interest/arousal disorder is characterized by lack of, or significantly reduced, sexual interest and/or arousal. Diagnosis requires ruling out psychological, medical, and substance/medication-related causes and relationship problems.

References

- Hypoactive sexual desire disorder: International Society for the Study of Women's Sexual Health (ISSWSH) Expert Consensus Panel Review.

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Female sexual interest/arousal disorder is characterized by lack of, or significantly reduced, sexual interest and/or arousal. Diagnosis requires ruling out psychological, medical, and substance/medication-related causes and relationship problems.

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Behavioral science	Psychiatric/Behavioral & Substance Abuse	Female sexual dysfunction
Subject	System	Topic

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A 45-year-old man comes to the office due to fatigue, lack of sexual desire, and inability to maintain an erection. A year ago, he was advised to lose weight with diet and exercise due to mildly elevated fasting glucose levels. The patient has smoked a pack of cigarettes daily for the past 20 years and drinks an alcoholic beverage 3-4 times per month. Blood pressure is 110/70 mm Hg and pulse is 65/min. Oxygen saturation is 99% on room air. BMI is 29 kg/m^2. Skin examination shows increased pigmentation over the knuckles and face. The liver is palpable 3-4 cm below the right costal margin. The remainder of the examination reveals small testes. Which of the following is most likely contributing to the development of the patient's symptoms?

A. Aortoiliac atherosclerosis

B. Autoimmune adrenalitis

C. Ectopic ACTH production

D. Fibrosis of the seminiferous tubules

E. Iron deposition in the pituitary gland

Submit

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- A. Aortoiliac atherosclerosis (4%)
- B. Autoimmune adrenalitis (16%)
- C. Ectopic ACTH production (22%)
- D. Fibrosis of the seminiferous tubules (3%)
- ✓ E. Iron deposition in the pituitary gland (53%)

Omitted
Correct answer
E

Collecting Statistics

01 sec
Time Spent

07/05/2020
Last Updated

Explanation

Clinical manifestations of hereditary hemochromatosis	
Skin	• Hyperpigmentation

Clinical manifestations of hereditary hemochromatosis	
Skin	• Hyperpigmentation
Musculoskeletal	• Arthritis (particularly 2nd & 3rd MCP joints) • Chondrocalcinosis
Gastrointestinal	• Elevated liver enzymes, hepatomegaly (early) • Cirrhosis & hepatocellular carcinoma (late)
Endocrine	• Diabetes mellitus • Hypopituitarism (eg, secondary hypogonadism, hypothyroidism)
Cardiac	• Restrictive or dilated cardiomyopathy • Conduction abnormalities

MCP = metacarpophalangeal

This patient's decreased libido, erectile dysfunction, and testicular atrophy are indicative of **hypogonadism**. These findings, in combination with **hyperpigmentation** of the skin, **elevated glucose**/diabetes mellitus, and **hepatomegaly**, are strongly suggestive of **hereditary hemochromatosis** (HH).

HH is an autosomal recessive disorder characterized by excessive intestinal iron absorption and accumulation in various tissues. **Secondary hypogonadism** occurs in HH due to **deposition of iron in the pituitary gland**, resulting in decreased gonadotropin secretion and subsequent testicular failure. In women, HH is often not diagnosed until after menopause, as premenopausal women have ongoing menstrual blood loss that usually prevents significant iron overload and symptom development; therefore, amenorrhea is a rare finding in women with HH.

(Choice A) Atherosclerotic disease is a common cause of erectile dysfunction in older men, especially those with a history of smoking, but it typically would not affect libido and would not cause hyperpigmentation or hepatomegaly.

(Choice B) Autoimmune adrenalitis is a common cause of primary adrenal insufficiency (ie, Addison disease). Hyperpigmentation is common

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(Choice C) Ectopic ACTH secretion causes paraneoplastic Cushing syndrome (eg, small cell lung cancer). Patients may develop hyperpigmentation and hyperglycemia but also often have hypertension and proximal muscle weakness. Small testes are not seen.

(Choice D) Testicular fibrosis is a common manifestation of Klinefelter syndrome (KS). Hypogonadism due to KS is typically apparent at puberty and is often associated with a eunuchoid habitus, sparse body hair, and high-pitched voice. Hepatomegaly is not common.

Educational objective:
Hereditary hemochromatosis can cause secondary hypogonadism due to deposition of iron in the pituitary gland, resulting in decreased gonadotropin secretion. Patients who develop secondary hypogonadism are also at risk for deficiencies in other pituitary hormones (eg, central hypothyroidism).

Pathology	Male Reproductive System	Hemochromatosis
Subject	System	Topic

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Pathology	Male Reproductive System	Hemochromatosis
Subject	System	Topic

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A 28-year-old professional athlete participates in a sports physiology study. She runs on a treadmill at an incrementally increasing speed. After 15-minutes, her pulse is 90% of the maximal heart rate based on her age, and several physiologic parameters are measured. Which of the following changes have most likely occurred compared to at rest?

	Minute ventilation	Ventilation/perfusion ratio	Mixed venous oxygen content
A.	Decreased	Increased	Unchanged
B.	Increased	Decreased	Decreased
C.	Increased	Increased	Decreased
D.	Increased	Unchanged	Increased
E.	Unchanged	Unchanged	Increased

Submit

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	Minute ventilation	Ventilation/perfusion ratio	Mixed venous oxygen content
A. (1%)	Decreased	Increased	Unchanged
B. (20%)	Increased	Decreased	Decreased
✓ C. (56%)	Increased	Increased	Decreased
D. (20%)	Increased	Unchanged	Increased
E. (0%)	Unchanged	Unchanged	Increased

Omitted
Correct answer
C

56%
Answered correctly

02 secs
Time Spent

06/30/2020
Last Updated

Explanation

Explanation

During **exercise**, respiratory activity changes to help meet the body's **increased metabolic demand**:

- **Increased minute ventilation** occurs via an increase in respiratory rate and tidal volume and facilitates an increased rate of **oxygen uptake** and **carbon dioxide removal**. The increase in tidal volume can reach up to 50% of resting vital capacity.
- The increased minute ventilation **increases alveolar ventilation** throughout the lungs. Pulmonary vascular resistance is reduced and cardiac output is increased, which allows for more evenly distributed blood flow throughout the lungs and **reduced physiologic dead space** (ie, reduction in the proportion of air in the respiratory tract that does not participate in gas exchange). Although blood flow through the lungs is increased, alveolar ventilation needs to increase more (blood flowing through the lungs during exercise is more deoxygenated than normal), resulting in an **increased ventilation-perfusion ratio**.

In addition, an accumulation of lactic acid decreases blood pH and stimulates a **rightward shift** in the hemoglobin dissociation curve, facilitating **increased unloading of oxygen** in skeletal muscle. Although increased cardiac output increases the rate of blood flow through the skeletal muscle capillaries and reduces the time allowed for oxygen unloading, the fraction of arterial oxygen extracted by skeletal muscle markedly increases during exercise, resulting in **decreased mixed venous oxygen content**.

These physiologic changes in the respiratory system that occur during exercise are most pronounced in highly trained athletes.

Educational objective:
Physiologic changes in the respiratory system that occur with exercise include increased minute ventilation (via both an increase in respiratory rate and tidal volume), reduced physiologic dead space, increased ventilation-perfusion ratio, and increased extraction of oxygen by skeletal muscle (resulting in decreased mixed venous oxygen content).

Physiology	Pulmonary & Critical Care	Physical exercise
Subject	System	Topic

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A 58-year-old man comes to the office due to worsening right upper extremity weakness over the past 4 weeks. The patient frequently travels for work and has had difficulty carrying heavy bags and getting luggage into or out of the overhead bins. He also has had neck and shoulder pain for the past several months, which he attributes to stress. The patient reports no trauma, and medical history is significant for hypertension. Physical examination shows weakness of shoulder abduction and loss of the biceps reflex on the right side. Pinprick sensation is decreased over the right lateral arm and forearm. Which of the following pathologic processes is most likely underlying this patient's current symptoms?

A. Axonal loss in the corticospinal tracts

B. Cystic expansion of the central canal

C. Degenerative changes in the vertebral joints

D. Microinjury and tear of the rotator cuff tendons

E. Rupture of the long head of the biceps tendon

Submit

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- A. Axonal loss in the corticospinal tracts (7%)
- B. Cystic expansion of the central canal (16%)
- ✓ C. Degenerative changes in the vertebral joints (55%)
- D. Microinjury and tear of the rotator cuff tendons (15%)
- E. Rupture of the long head of the biceps tendon (5%)

Omitted
Correct answer
C

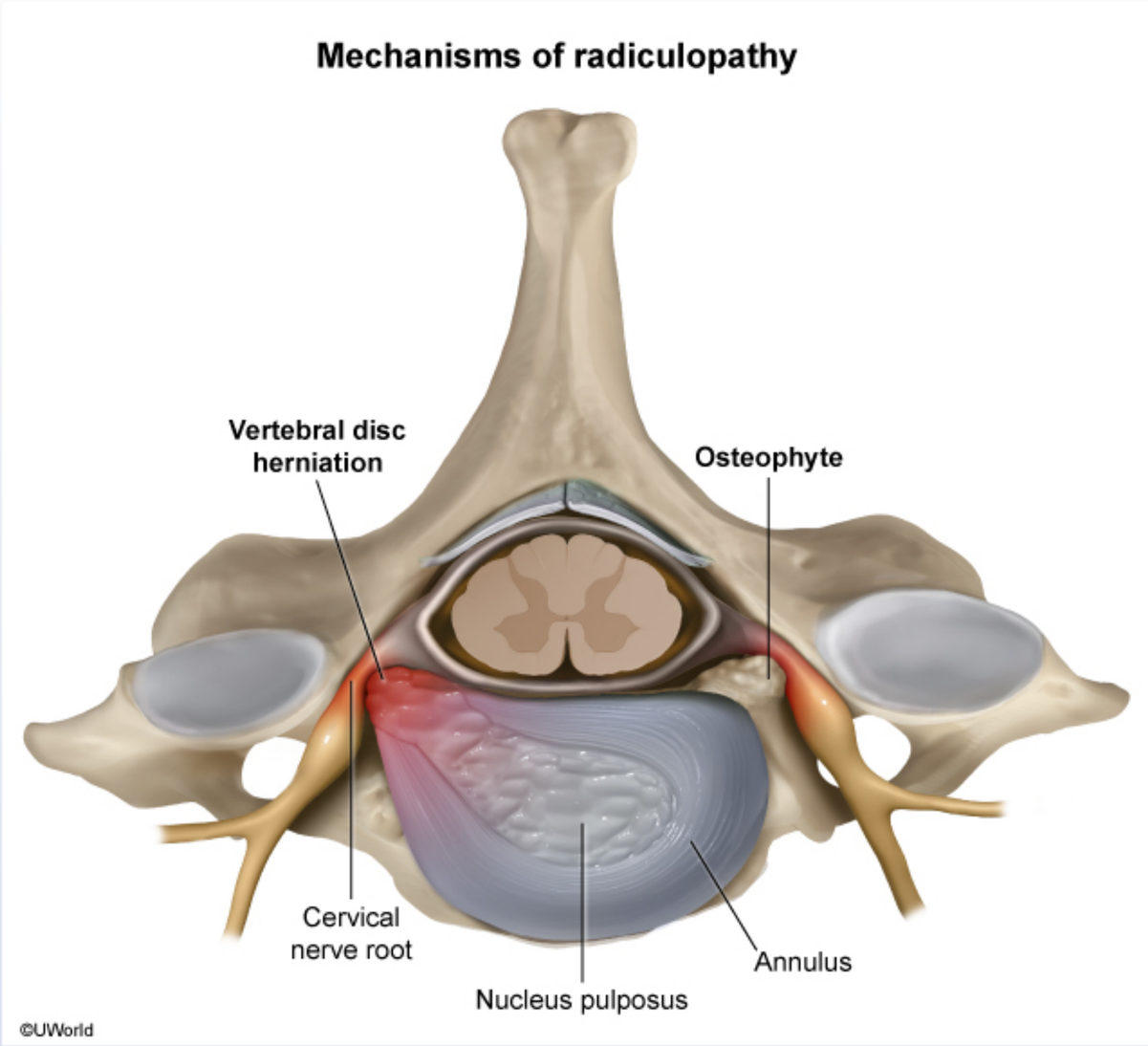
55%
Answered correctly

01 sec
Time Spent

07/03/2020
Last Updated

Explanation

Mechanisms of radiculopathy



This patient's sensory (eg, lateral arm/forearm sensation loss) and motor deficits (eg, impaired shoulder abduction, biceps reflex) are not isolated

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This patient's sensory (eg, lateral arm/forearm sensation loss) and motor deficits (eg, impaired shoulder abduction, biceps reflex) are not isolated to the distribution of a single peripheral nerve (eg, median, ulnar), but rather follow the **C5 dermatomal and myotomal distribution**, indicating **cervical radiculopathy**.

The manifestations of cervical radiculopathies vary depending on the affected nerve root but typically present with **neck or arm pain** associated with motor and/or sensory deficits. Radiculopathies occur due to **compression of spinal nerve roots**, which is most commonly due to either:

- **Spinal spondylosis:** Aging leads to **degeneration** of the vertebral bodies, discs, and joints. Disc space decreases, and joint stress results in osteophyte (eg, bone spur) formation, which slowly narrows the neural foramina and leads to a **subacute onset** of symptoms (as seen in this patient).
- **Vertebral disc herniation:** Degeneration of ligamentous fibers can lead to a tear in the intervertebral disc annulus, resulting in herniation of the nucleus pulposus with potential nerve root compression. Disc rupture typically occurs acutely (eg, during weight lifting).

(Choice A) Axonal loss in the corticospinal tracts occurs in amyotrophic lateral sclerosis, a neurodegenerative disease that affects both upper and lower motor neurons. Although it can result in weakness and atrophy, it would also result in upper motor neuron signs (eg, hyperreflexia), and sensory disturbances would be atypical.

(Choice B) Syringomyelia results from cystic expansion of the central canal in the spinal cord. This can result in upper extremity weakness and sensory deficits, but because it expands from the central portion of the spinal cord, both upper extremities are typically affected, most often in a "cape" distribution.

(Choice D) Microinjury and tear of the rotator cuff tendons can result in weakness of shoulder abduction. However, sensory deficits are unexpected.

(Choice E) Rupture of the long head of the biceps tendon could result in shoulder pain that is aggravated by repetitive overhead activities; a loss of the biceps reflex may be observed if the rupture is complete. However, it would not cause weakness of shoulder abduction (biceps flexes and supinates the forearm) and sensory deficits would not be present.

Educational objective:

cervical radiculopathy.

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Educational objective:
Cervical radiculopathy typically results in neck and/or arm pain associated with neurologic deficits that follow a dermatomal/myotomal pattern. Osteophytes that form due to degenerative changes in the vertebral joints can progressively narrow the neural foramina leading to nerve root compression.

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Anatomy	Nervous System	Radiculopathy
Subject	System	Topic

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This patient's sensory (eg ... ed
to the distribution of a sing ...
cervical radiculopathy.

The manifestations of cer ... d
with motor and/or sensory ...

- **Spinal spondylosis** ... ults
  in osteophyte (eg, b ... n in
  this patient).
- **Vertebral disc herr** ... n of
  the nucleus pulposu ...

(Choice A) Axonal loss i ... and
lower motor neurons. Alth ...
sensory disturbances wou ...

(Choice B) Syringomyelia ... nd
sensory deficits, but becau ... a
"cape" distribution.

Exhibit Display

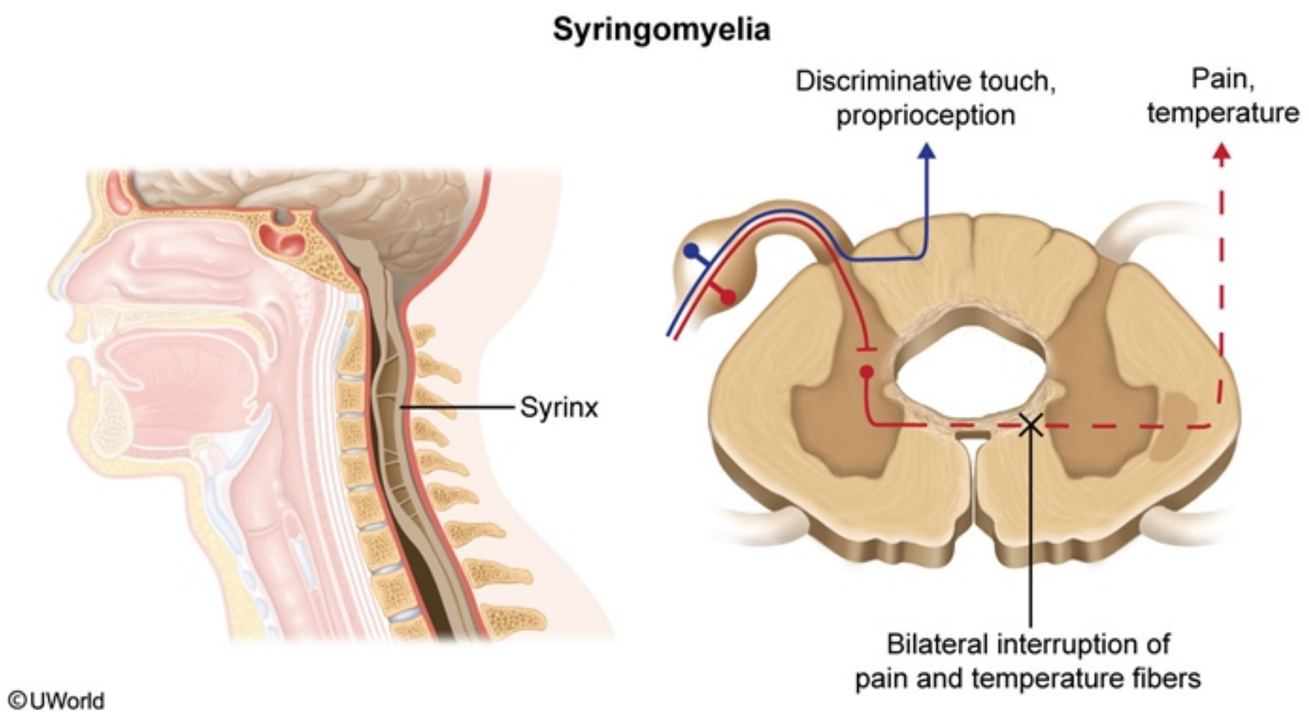
Features of cervical radiculopathy

Nerve root (Disc space)	Reflex affected	Sensory loss*	Weakness
C5 (C4-5)	• Biceps	• Lateral upper arm	• Shoulder abduction (deltoid) • Elbow flexion (biceps)
C6 (C5-6)	• Biceps • Brachioradialis	• Thumb • Index finger	• Elbow flexion (biceps) • Forearm pronation/supination (brachioradialis) • Wrist extension
C7 (C6-7)	• Triceps	• Dorsal forearm • Middle finger	• Elbow extension (triceps) • Wrist flexion • Finger extension
C8 (C7-T1)	• Finger flexors**	• Ring & little fingers	• Finger flexion & extension • Thumb flexion & abduction
T1 (T1-2)	• Finger flexors**	• Medial forearm	• Finger abduction & adduction

*In addition to neck/shoulder pain, radicular pain typically has a similar distribution to sensory loss.
**Not typically evaluated clinically.

Add To Flash Card

Exhibit Display



Zoom In | Zoom Out | Reset | Add To Flash Card

cape distribution.

Settings

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30

Item 5 of 32
Question Id: 14895

Mark | Previous | Next | Full Screen | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom | Settings

A 30-year-old primigravid woman at 35 weeks gestation comes to the emergency department due to fever, nausea, vomiting, watery diarrhea, and myalgias that began one day ago. She has no contractions, vaginal bleeding, or leakage of fluid. Temperature is 39.3 C (102.7 F), blood pressure is 90/60 mm Hg, and pulse is 126/min. The abdomen is soft, and the uterus is nontender. Fetal heart rate is 180/min on Doppler ultrasound. The remainder of the physical examination is normal. Blood cultures grow gram-positive rods. Which of the following is the major virulence factor of the organism responsible for this patient's clinical presentation?

- A. Cytotoxin that creates pores in phagosomes
- B. Endotoxin-mediated complement and tissue factor activation
- C. Exotoxin inhibition of neurotransmitter release
- D. Exotoxin-mediated inhibition of elongation factor

Submit

Block Time Remaining: 00:02:25
TUTOR

0 | Feedback | Suspend | End Block

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- ✓ A. Cytotoxin that creates pores in phagosomes (44%)
- B. Endotoxin-mediated complement and tissue factor activation (30%)
- C. Exotoxin inhibition of neurotransmitter release (7%)
- D. Exotoxin-mediated inhibition of elongation factor (18%)

Omitted
Correct answer
A

44%
Answered correctly

02 secs
Time Spent

06/20/2020
Last Updated

Explanation

Gram-positive rods in blood cultures
• *Corynebacterium* species (diphtheroid) • *Clostridium* species • *Nocardia* species or the anaerobic *Actinomyces* species • *Listeria* species

Gram-positive rods in blood cultures
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This pregnant woman has **febrile gastroenteritis** (eg, fever, vomiting, diarrhea) and **gram-positive rods** in her bloodstream, raising strong suspicion for ***Listeria monocytogenes*** infection. *L monocytogenes* is a motile, **facultatively intracellular** organism with several unique adaptations that allow it to evade the host immune response, including the following:

- **Listeriolysin O**: This major virulence factor generates **pores in phagosome** membranes, which allows phagocytosed *L monocytogenes* to **escape into the cytoplasm** of monocytes and avoid lysosomal destruction.
- **Actin-based transcellular spread**: The organism hijacks the actin-based cellular motility mechanism of host cells, which allows it to spread to adjacent cells without reentering the extracellular space. This significantly reduces exposure of *L monocytogenes* to antibodies and phagocytic cells.

Because of these adaptations, antibody- and phagocyte-mediated destruction of the pathogen is impaired; therefore, infections are controlled primarily by the cytotoxic T-cell response.

Most *L monocytogenes* infections occur in **pregnant women** in the third trimester. Although antibiotics are curative, *L monocytogenes* quickly invades the placenta and may cause fetal death, premature birth, and neonatal infection.

(Choice B) Bacterial lipopolysaccharide (endotoxin) is the major component of the cell wall in gram-negative, not gram-positive, bacteria (some sources erroneously report that *L monocytogenes* contains lipopolysaccharide). Endotoxin activates complement, coagulation, and fibrinolysis, which can lead to septic shock and disseminated intravascular coagulation.

(Choice C) *Clostridium botulinum*, an anaerobic gram-positive rod, produces an exotoxin (botulinum toxin) that inhibits the synaptic transmission of motor neurons. Patients typically develop descending, symmetric motor deficits; minimal sensory changes; and no fever.

- **Actin-based transcellular spread**: The organism hijacks the actin-based cellular motility mechanism of host cells, which allows it to spread to adjacent cells without reentering the extracellular space. This significantly reduces exposure of *L monocytogenes* to antibodies and phagocytic cells.

Because of these adaptations, antibody- and phagocyte-mediated destruction of the pathogen is impaired; therefore, infections are controlled primarily by the cytotoxic T-cell response.

Most *L monocytogenes* infections occur in **pregnant women** in the third trimester. Although antibiotics are curative, *L monocytogenes* quickly invades the placenta and may cause fetal death, premature birth, and neonatal infection.

(Choice B) Bacterial lipopolysaccharide (endotoxin) is the major component of the cell wall in gram-negative, not gram-positive, bacteria (some sources erroneously report that *L monocytogenes* contains lipopolysaccharide). Endotoxin activates complement, coagulation, and fibrinolysis, which can lead to septic shock and disseminated intravascular coagulation.

(Choice C) *Clostridium botulinum*, an anaerobic gram-positive rod, produces an exotoxin (botulinum toxin) that inhibits the synaptic transmission of motor neurons. Patients typically develop descending, symmetric motor deficits; minimal sensory changes; and no fever.

(Choice D) Pathogenic strains of *Corynebacterium diphtheriae* produce an exotoxin that inhibits elongation factor in host cells, which causes pseudomembranous pharyngitis and myocarditis. Although *C diphtheriae* is a gram-positive rod, it does not cause febrile gastroenteritis.

Educational objective:
Listeria monocytogenes is a facultative intracellular, gram-positive rod that most often causes febrile gastroenteritis. Pathogenesis is mediated largely by listeriolysin O, an enzyme that creates pores in phagosomes, which allows the bacteria to escape lysosomal destruction. Pregnant women in the third trimester are at greatest risk; infection increases the risk of fetal demise, early labor, and neonatal infection.

Microbiology	Infectious Diseases	Listeria
Subject	System	Topic

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A 32-year-old man comes to the office due to a substernal burning sensation that has been occurring intermittently over the last 6 months. The sensation worsens with spicy and fatty meals and is associated with food regurgitation and a sour taste in the back of the throat. He has no projectile vomiting, dysphagia, or unexpected weight loss. Medical history is significant for cystic fibrosis complicated by pancreatic insufficiency, for which the patient takes pancreatic enzyme replacement therapy with all meals. Vital signs are within normal limits. The abdomen is soft and nontender. He is prescribed omeprazole with subsequent improvement in his gastroesophageal reflux symptoms. In this patient, absorption of which of the following nutrients will likely improve due to initiation of this new medication?

A. Amino acids

B. Calcium

C. Dietary fat

D. Iron

E. Magnesium

Submit

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A. Amino acids (21%)
B. Calcium (13%)
✓ C. Dietary fat (37%)
D. Iron (19%)
E. Magnesium (8%)

Omitted
Correct answer
C

37%
Answered correctly

01 sec
Time Spent

06/29/2020
Last Updated

Explanation

Proton pump inhibitors	
Mechanism of action	• Irreversible inhibition of parietal cell hydrogen-potassium-ATPase

Proton pump inhibitors	
Mechanism of action	• Irreversible inhibition of parietal cell hydrogen-potassium-ATPase
Common uses	• Gastroesophageal reflux disease • Peptic ulcer disease
Adverse effects	• Malabsorption of calcium, iron, magnesium & vitamin B_{12} ◦ Enhances fat absorption in patients given pancreatic enzyme replacement therapy • Increases risk of infection (eg, *Clostridioides* [formerly *Clostridium*] *difficile*, pneumonia) • Osteoporosis, chronic kidney disease, SIBO

SIBO = small intestinal bacterial overgrowth.

This patient with heartburn and regurgitation has the classic manifestations of gastroesophageal reflux disease, a common disorder that occurs when gastric acid refluxes into the esophagus. The mainstay of therapy is gastric acid suppression, usually with **proton pump inhibitors** (PPIs) (eg, pantoprazole, omeprazole).

PPIs irreversibly inhibit the hydrogen-potassium-ATPase pump found in parietal cells, thereby inhibiting hydrochloric acid secretion into the stomach lumen. Although this effectively raises the stomach pH and prevents gastric acid irritation of the esophagus, the acidic environment of the stomach is necessary to absorb certain nutrients. Therefore, common adverse effects of PPIs include malabsorption of calcium, iron, magnesium, and vitamin B_{12} **(Choices B, D, and E)**.

Patients with **pancreatic insufficiency** (eg, cystic fibrosis, chronic pancreatitis) cannot synthesize the pancreatic enzymes required for digestion of protein, fat, and carbohydrates. As such, the condition is managed with pancreatic enzyme replacements, which contain varying amounts of lipase, amylase, and protease. Unlike amylase and protease, which are activated by the low pH of the stomach, **lipase**, which plays a vital role in fat digestion, is **inactivated by the acidic environment** of the stomach. Therefore, by decreasing gastric hydrochloric acid production, **PPI use increases lipase activity** (ie, it prevents exogenous lipase from being denatured as it passes through the stomach), **enhancing fat absorption** in

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(Choice A) Protein digestion of amino acids requires the activity of a protease known as pepsin, which is more active at low pH. Although one might expect the elevated stomach pH to inhibit protein absorption, chronic PPI use has not been associated with protein malabsorption (likely due to functional overlap with pancreatic and enteric proteases).

Educational objective:
Proton pump inhibitors (PPI) prevent the hydrogen-potassium-ATPase pump found in parietal cells from releasing hydrochloric acid into the stomach lumen. Chronic PPI use protects exogenously administered lipase and enhances fat absorption in patients dependent on pancreatic enzyme replacement therapy.

References

- Optimising the therapy of exocrine pancreatic insufficiency by the association of a proton pump inhibitor to enteric coated pancreatic extracts.
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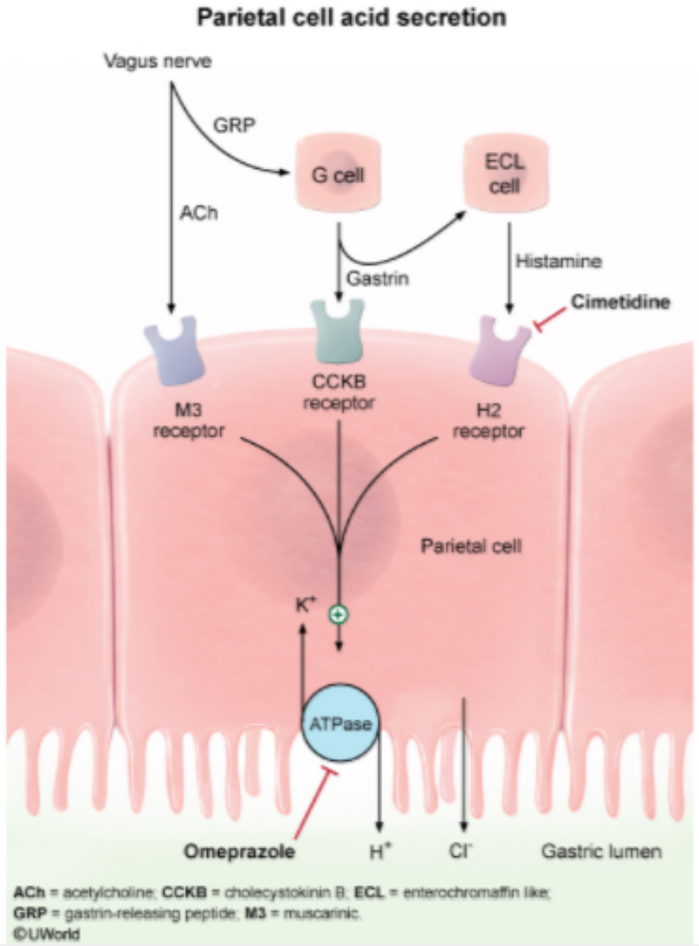
Exhibit Display



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Pharmacology	Gastrointestinal & Nutrition	Proton pump inhibitors
Subject	System	Topic

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A 46-year-old man experiences burning pain in his left thigh and leg. The next day, he notices groups of erythematous, tender, fluid-filled vesicles in the painful region. The lesions gradually crust over the next several days as shown in the exhibit. Which of the following dermatomes are most likely involved in this patient's disease process?

- A. L1-L2
- B. L3-L4
- C. L5-S1
- D. S2-S3
- E. No specific dermatome pattern

Submit

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- A. L1-L2 (18%)
- ✓ B. L3-L4 (62%)
- C. L5-S1 (9%)
- D. S2-S3 (3%)
- E. No specific dermatome pattern (7%)

Omitted
Correct answer
B

62%
Answered correctly

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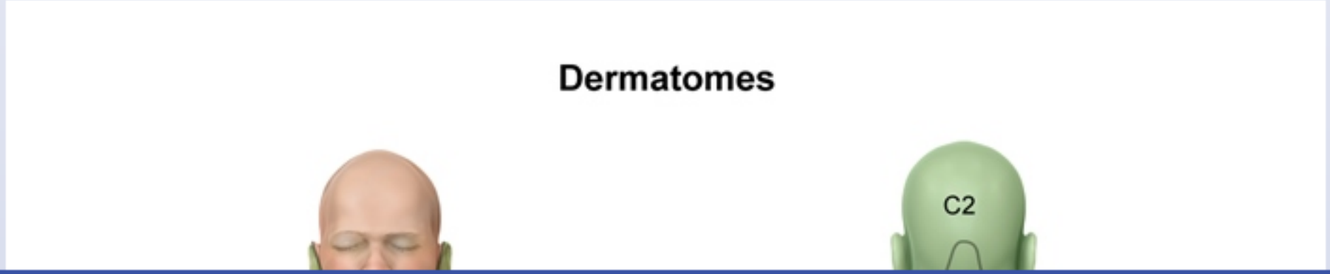
07/03/2020
Last Updated

Explanation



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Item 7 of 32
Question Id: 19688

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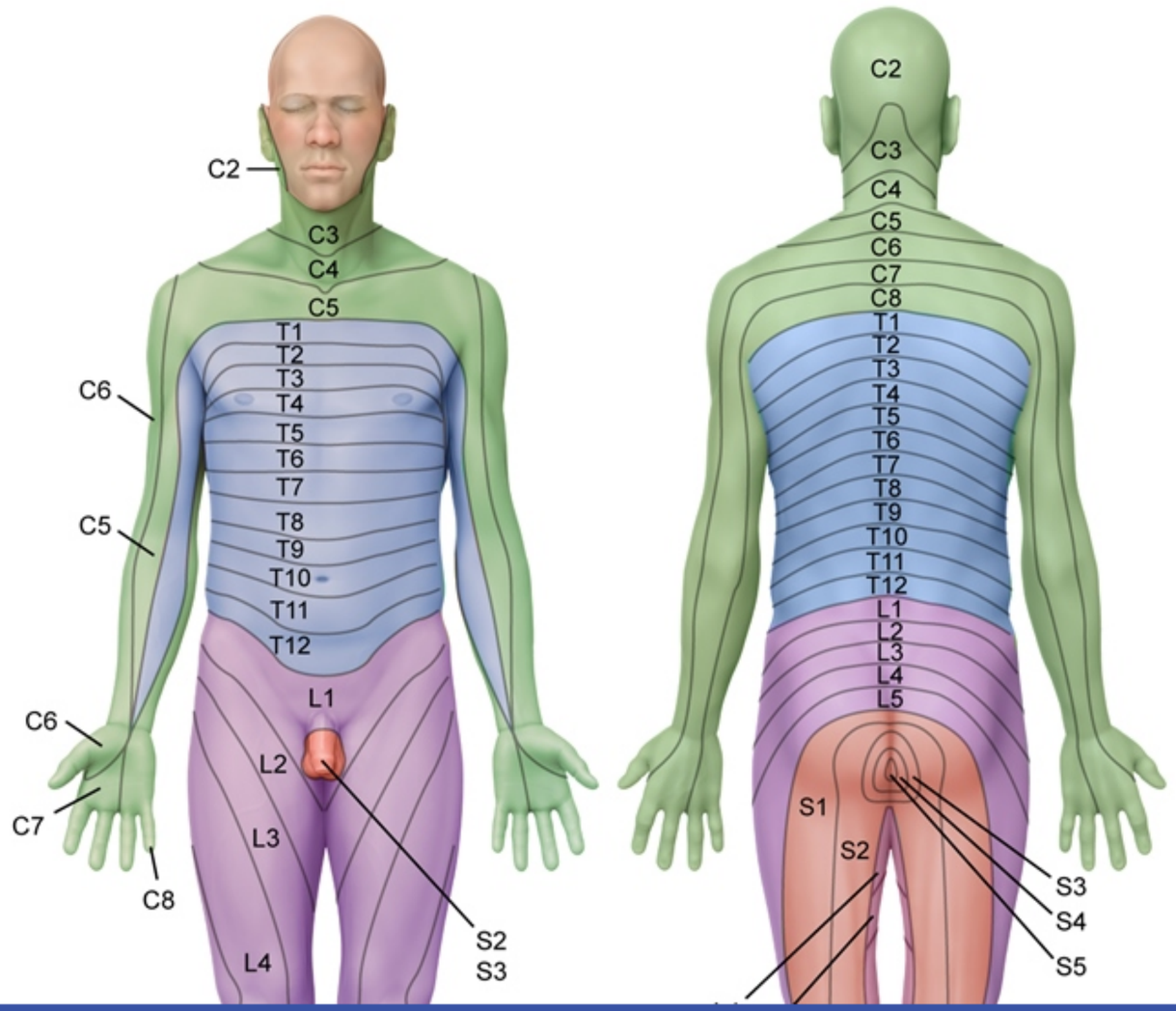
Dermatomes



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Item 7 of 32
Question Id: 19688

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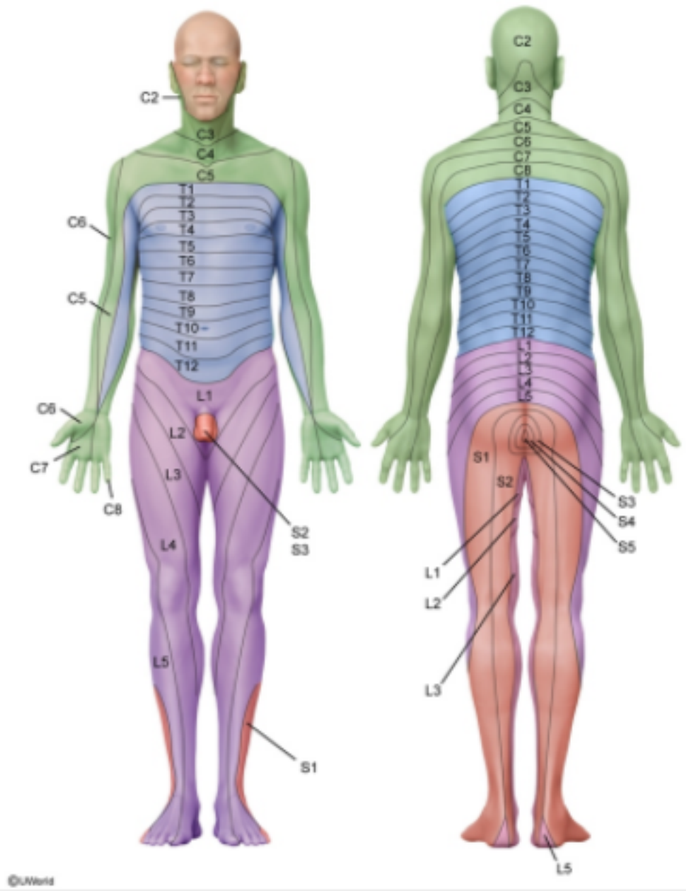
Exhibit Display

Dermatomes



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L5

This patient has single and grouped vesicles in various stages of ulceration and crusting, which is consistent with **herpes zoster** (ie, shingles). Following primary VZV infection (ie, chickenpox), the virus migrates via sensory nerves to the **dorsal spinal ganglia**, where it lies dormant for years. Reactivation of the virus typically occurs in a single (or multiple-adjacent) ganglion. This causes hemorrhagic inflammation involving the entire peripheral nerve associated with that ganglion and eruption of a painful, vesicular rash on the skin supplied by that sensory nerve (ie, **dermatome**).

This patient's vesicular rash primarily involves the **anteromedial thigh** and **medial leg**, which is consistent with the dermatomal distribution of **L3 and L4**.

(Choice A) The L1 dermatome is at the level of the inguinal ligament. The L2 dermatome covers the upper anteromedial thigh but does not extend downward into the leg.

(Choice C) The L5 dermatome covers the lateral thigh and anterolateral leg along with the dorsum/sole of the foot. The S1 dermatome includes the posterior thigh and leg and the lateral portion of the foot.

(Choice D) The S2 dermatome supplies portions of the posterior thigh and leg as well as the perineum. S3 primarily supplies the perineum.

(Choice E) Primary VZV infection (ie, chickenpox) produces a generalized vesicular rash. However, reactivation typically occurs in a single (or multiple-adjacent) spinal ganglia, leading to a rash confined to the distribution of those nerves (ie, dermatome).

Educational objective:
Herpes zoster reactivation typically occurs in a single or multiple-adjacent dorsal spinal ganglia, leading to a vesicular rash in a dermatomal distribution. The L3 and L4 dermatomes supply the anteromedial thigh and medial leg.

Anatomy	Nervous System	Herpes zoster
Subject	System	Topic

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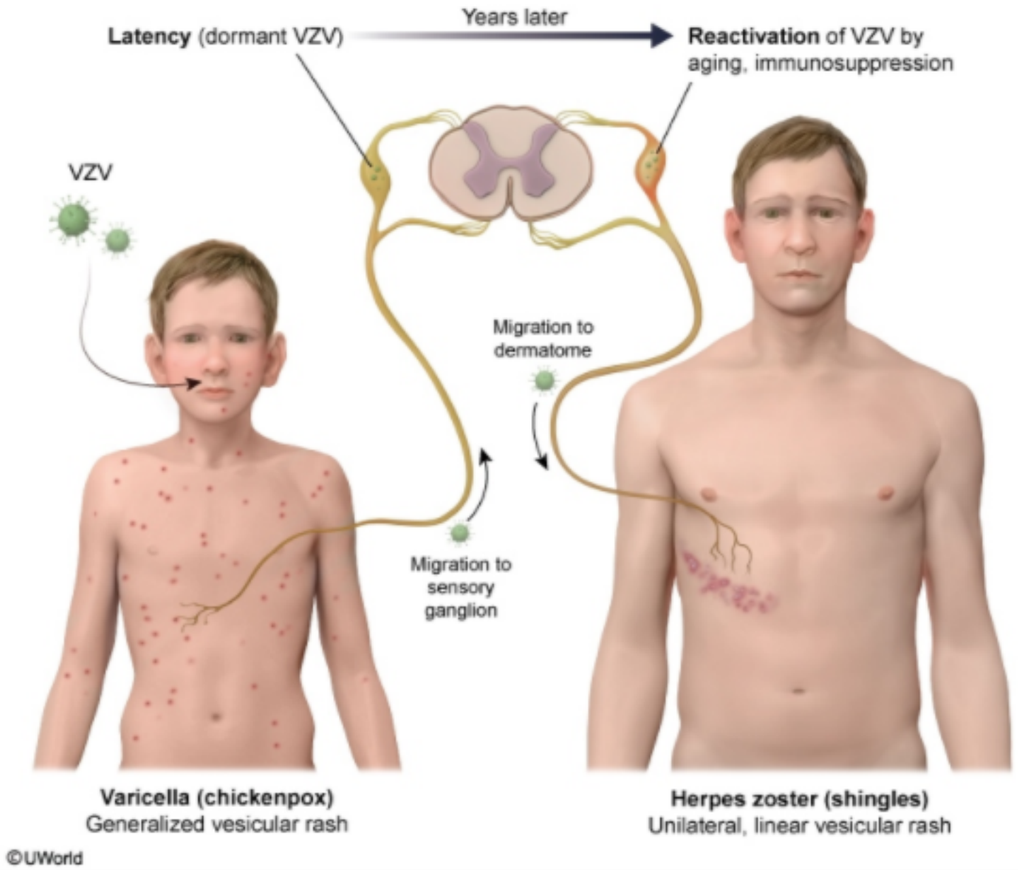
L5

Exhibit Display

Varicella-zoster virus (VZV) infection



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A 16-year-old boy is brought to the office by his parents due to tremors and difficulty walking. Over the past year, his school performance has declined, and he has been moodier and more impulsive. His parents also note that he has been sleeping more than usual and has had a poor appetite for the past 2 months. Approximately 3 weeks ago, the patient developed a tremor in both hands that is most prominent when he reaches for an object or tries to write. The tremor has worsened significantly over the past week, and he has developed an unsteady, broad-based gait. Laboratory studies reveal elevated serum transaminases and 24-hour urinary copper excretion. The patient is prescribed penicillamine therapy. This medication primarily works through which of the following mechanisms?

- A. Decreasing intestinal absorption of copper
- B. Increasing urinary excretion of copper
- C. Repletion of intracellular glutathione
- D. Stimulation of defective gene expression
- E. Stimulation of canalicular transport proteins

Submit

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- A. Decreasing intestinal absorption of copper (36%)
- ✓ B. Increasing urinary excretion of copper (58%)
- C. Repletion of intracellular glutathione (2%)
- D. Stimulation of defective gene expression (0%)
- E. Stimulation of canalicular transport proteins (3%)

Omitted
Correct answer
B

58%
Answered correctly

02 secs
Time Spent

07/01/2020
Last Updated

Explanation

Wilson disease	
	• Autosomal recessive mutation of *ATP7B* → hepatic copper

Wilson disease	
Pathogenesis	• Autosomal recessive mutation of *ATP7B* → hepatic copper accumulation → leak from damaged hepatocytes → deposits in tissues (eg, basal ganglia, cornea)
Clinical findings	• Hepatic (acute liver failure, chronic hepatitis, cirrhosis) • Neurologic (parkinsonism, gait disturbance, dysarthria) • Psychiatric (depression, personality changes, psychosis)
Diagnosis	• ↓ Ceruloplasmin & ↑ urinary copper excretion • Kayser-Fleischer rings on slit-lamp examination • ↑ Copper content on liver biopsy
Treatment	• Chelators (eg, D-penicillamine, trientine) • Zinc (interferes with copper absorption)

This patient has **Wilson disease**, an autosomal recessive disorder characterized by excessive copper deposition in the liver, basal ganglia, and cornea.

Copper is an essential nutrient that is absorbed in the intestines, metabolized by hepatocytes, and excreted in the bile. Pathogenesis of Wilson disease involves impaired hepatocellular copper transport, which results in **decreased biliary excretion of copper**. The resultant increase in intracellular copper causes oxidative stress and apoptosis of hepatocytes, which leads to liver dysfunction (eg, elevated transaminases, liver failure). Excess copper is then released into the bloodstream and deposited into extrahepatic tissues, causing neurologic (eg, tremor, ataxia) and psychiatric symptoms (eg, impulsivity, depressive symptoms). Although renal excretion of copper in healthy patients is extremely low, the relative increase in serum copper in Wilson disease results in increased urinary excretion of copper, as seen in this patient.

First-line treatment of Wilson disease is with **penicillamine**, a **copper chelating agent**. Penicillamine binds free copper as well as reduces copper bound to other proteins. This reduction preferentially increases affinity of copper to the chelating agent. The chelator-copper complex is soluble, thereby **increasing urinary copper excretion**.

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(Choice A) Zinc decreases intestinal absorption of copper and can be used in conjunction with penicillamine to treat Wilson disease.

(Choice C) Acetaminophen overdose causes hepatotoxicity via depletion of intracellular glutathione, which can be reversed with N-acetylcysteine treatment.

(Choices D and E) Gene therapy could theoretically improve or cure Wilson disease by transferring a functional copper transport protein gene into hepatocytes. This would restore their ability to transport excess copper into secretory vesicles, promoting exocytosis of copper into the bile canaliculi.

Educational objective:
Penicillamine, a first-line treatment for Wilson disease, is a copper chelating agent that increases the urinary excretion of copper.

References

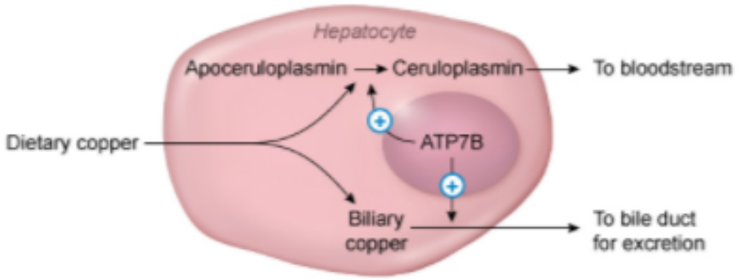
- Clinical management of Wilson disease.

Pharmacology Gastrointestinal & Nutrition Wilson disease

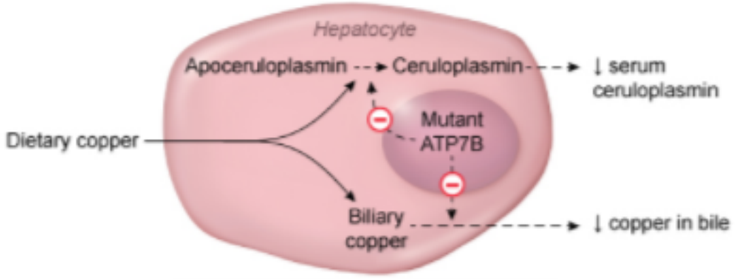
Exhibit Display

Copper metabolism and Wilson disease

Normal copper metabolism



Impaired copper metabolism in Wilson disease



↑ hepatocellular copper
↓
Oxidative stress, necrosis & apoptosis
↓
Release of free copper into bloodstream
↓
Extrahepatic copper deposition

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Pharmacology | Gastrointestinal & Nutrition | Wilson disease

A 15-year-old boy is evaluated for progressive lower extremity weakness. The patient has had difficulty running and keeping up with peers for the past several years and has sprained his ankles on multiple occasions. His father also experienced similar symptoms beginning at the same age and became wheelchair bound. Physical examination shows weakness and atrophy of the distal lower extremity muscles. There is bilateral pes cavus deformity. Ankle reflexes are absent, and sensation to vibration is also absent in the feet. Abnormal function of which of the following is the most likely cause of this patient's condition?

A. Muscle dystrophin

B. Myelin protein

C. Ryanodine receptors

D. Synaptic vesicles

E. Tau protein

Submit

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- A. Muscle dystrophin (36%)
- ✓ B. Myelin protein (54%)
- C. Ryanodine receptors (3%)
- D. Synaptic vesicles (4%)
- E. Tau protein (2%)

Omitted
Correct answer
B

54%
Answered correctly

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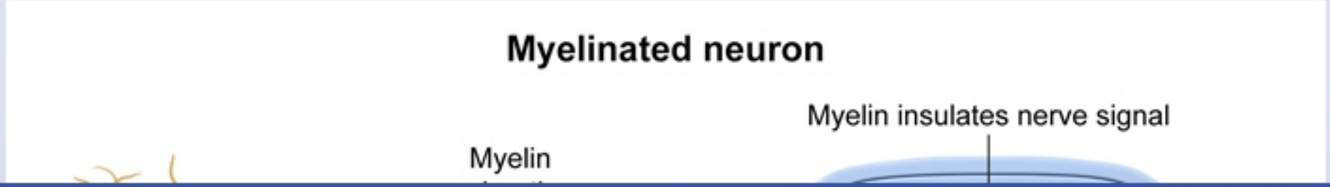
Time Spent

06/18/2020
Last Updated

Explanation



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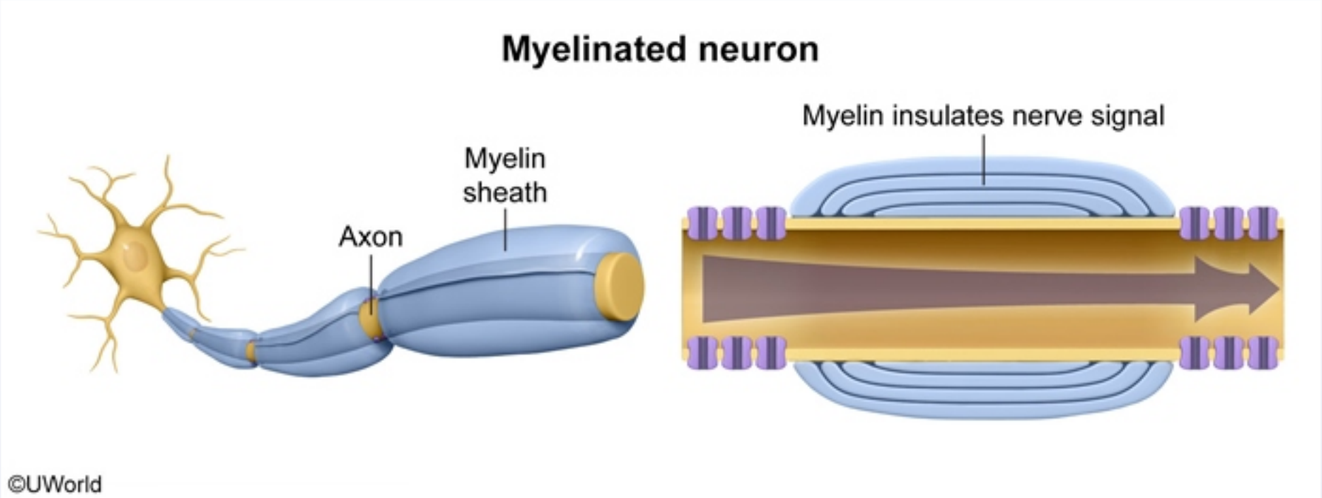

This adolescent with lower extremity weakness, muscle atrophy, and peripheral neuropathy (ie, decreased vibratory sense, absent ankle reflex) likely has **Charcot-Marie-Tooth disease (CMT)**. CMT is a group of **hereditary peripheral neuropathies** characterized by mutations in genes coding for peripheral nerve axonal or **myelin proteins**. The most common subtype, CMT1, occurs due to an autosomal dominant mutation in the *PMP22* gene.

Manifestations of CMT depend on the underlying genetic abnormality; however, most cases present in **adolescence** or early adulthood with progressive, symmetric **distal muscle atrophy** and **weakness**. Initial manifestations often include frequent **ankle sprains** or difficulty with exercise. Physical examination typically demonstrates muscle wasting most prominent in the distal lower extremities, with **sensory loss, areflexia, pes cavus** (ie, high arches), and hammer toes. Upper extremity involvement (ie, intrinsic musculature of the hands) typically occurs later in the disease course.

(Choice A) Duchenne and Becker muscular dystrophy are X-linked inherited disorders caused by abnormalities in muscle dystrophin. Patients also develop distal limb weakness but present with a waddling gait and pseudohypertrophy (rather than atrophy) of the calf muscles.

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(Choice D) Botulinum toxin cleaves SNARE proteins within neurons, preventing the synaptic vesicle from fusing to the cell membrane and releasing neurotransmitters. Botulism typically causes acute-onset cranial neuropathies (eg, dysarthria, ptosis) and descending muscle weakness after toxin ingestion (eg, eating contaminated home-canned food) or spore exposure (eg, giving honey to an infant). Muscle wasting is unexpected.

(Choice E) Hyperphosphorylated tau protein is seen in multiple neurodegenerative diseases (eg, Alzheimer dementia, frontotemporal dementia). These typically occur in elderly patients and present with progressive impairments in cognitive function, not muscle atrophy.

Educational objective:
Charcot-Marie-Tooth is a group of hereditary peripheral neuropathies characterized by mutations in genes coding for peripheral nerve axonal or myelin proteins. Manifestations typically include progressive, symmetric distal muscle atrophy and weakness most prominent in the feet and calf musculature, with sensory loss, areflexia, pes cavus (ie, high arches), and hammer toes.

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Pathology	Nervous System	Charcot marie tooth disease
Subject	System	Topic

A study examined the effect of a low-carbohydrate diet compared to a low-fat diet on body weight. A sample of 150 overweight but otherwise healthy adults from a large city was enrolled in the study and randomly assigned in a 1:1 ratio to either the low-carbohydrate (40 g/d) or the low-fat (<7% saturated fat) diet. At 12 months, a greater body weight change was reported in the low-carbohydrate diet group compared to the low-fat diet group, with a mean difference in body weight change of −3.5 kg ($p = 0.01$, predetermined significance level = 0.05). Which of the following is the most accurate interpretation of the results of this study?

A. The observed mean difference in body weight change of −3.5 kg is not statistically significant

B. The probability of observing a mean difference in body weight change of −3.5 kg is 0.01

C. There is a 1% chance of observing a mean difference in body weight change of at least −3.5 kg when no difference between groups is assumed

D. There is a 1% chance that an adult on a low-carbohydrate diet will have a body weight change of at least −3.5 kg at 12 months after starting the diet

E. There is a 1% chance that the mean difference in body weight change is biased in favor of the low-carbohydrate diet group

Submit

A study examined the effect of a low-carbohydrate diet compared to a low-fat diet on body weight. A sample of 150 overweight but otherwise healthy adults from a large city was enrolled in the study and randomly assigned in a 1:1 ratio to either the low-carbohydrate (40 g/d) or the low-fat (<7% saturated fat) diet. At 12 months, a greater body weight change was reported in the low-carbohydrate diet group compared to the low-fat diet group, with a mean difference in body weight change of −3.5 kg (p = 0.01, predetermined significance level = 0.05). Which of the following is the most accurate interpretation of the results of this study?

A. The observed mean difference in body weight change of −3.5 kg is not statistically significant (3%)

B. The probability of observing a mean difference in body weight change of −3.5 kg is 0.01 (5%)

✓ C. There is a 1% chance of observing a mean difference in body weight change of at least −3.5 kg when no difference between groups is assumed (57%)

D. There is a 1% chance that an adult on a low-carbohydrate diet will have a body weight change of at least −3.5 kg at 12 months after starting the diet (9%)

E. There is a 1% chance that the mean difference in body weight change is biased in favor of the low-carbohydrate diet group (24%)

Omitted
Correct answer
C

57%
Answered correctly

02 secs
Time Spent

06/22/2020
Last Updated

Explanation

Statistical tests contrast a null hypothesis (H_0) and an alternative hypothesis (H_a), in this case:

- H_0 is a claim of **no difference** between populations (eg, no difference in mean body weight between the low-carbohydrate population and the low-fat population)

Explanation

Statistical tests contrast a null hypothesis (H_0) and an alternative hypothesis (H_a), in this case:

- H_0 is a claim of **no difference** between populations (eg, no difference in mean body weight between the low-carbohydrate population and the low-fat population).
- H_a is a claim of a **difference** between populations (eg, difference in mean body weight between the 2 populations).

Statistical inference uses data from **samples** (eg, 75 adults in the low-carbohydrate sample, 75 adults in the low-fat sample) to draw conclusions about underlying **populations**. Sample estimates or differences (eg, sample mean, difference in mean between 2 samples) generally vary with distinct samples (eg, if a different sample of 75 adults was chosen for each group) and may be close but not equal to the underlying population value.

One way to account for **sampling variation** is to calculate the ***p*-value**, which is the **probability of obtaining a sample value at least as large as the one observed** when the population value claimed in **H_0 is assumed to be true**. The magnitude of the *p*-value compared to a predetermined significance level (eg, 0.05 [or 5%] commonly used as the threshold) determines whether there is convincing evidence against H_0.

- A low *p*-value (eg, <0.05) occurs when the sample value significantly disagrees with the population value claimed in H_0 and provides convincing evidence against H_0 (ie, H_0 is probably wrong). Results are considered statistically significant.
- A high *p*-value (eg, ≥0.05) occurs when the sample value is close to the population value claimed in H_0 and provides convincing evidence in favor of H_0 (ie, H_0 might be correct). Results are considered not statistically significant.

In this case, the given ***p*-value = 0.01**; therefore, there is a **1% chance** (ie, 0.01) of observing a mean difference in body weight change (ie, sample estimate) of **at least −3.5 kg** between the low-fat and the low-carbohydrate samples when **no difference between the populations is assumed** (ie, H_0 is assumed to be true) **(Choice B)**.

(Choices A, D, and E) The *p*-value of 0.01 is less than 0.05; therefore, the observed mean difference is statistically significant at the 5% level. The *p*-value is not associated with individual observations in a sample. It accounts for sampling variation (ie, random variation) not bias (ie, systematic variation).

Educational objective:

about underlying **populations**. Sample estimates or differences (eg, sample mean, difference in mean between 2 samples) generally vary with distinct samples (eg, if a different sample of 75 adults was chosen for each group) and may be close but not equal to the underlying population value.

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In this case, the given ***p*-value = 0.01**; therefore, there is a **1% chance** (ie, 0.01) of observing a mean difference in body weight change (ie, sample estimate) of **at least −3.5 kg** between the low-fat and the low-carbohydrate samples when **no difference between the populations is assumed** (ie, H_0 is assumed to be true) **(Choice B)**.

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Educational objective:
The *p*-value is the probability of obtaining a result (ie, sample estimate) at least as large as the one observed when the population value claimed in the null hypothesis is assumed to be true. A *p*-value <0.05 typically indicates that results are statistically significant.

Biostatistics	Biostatistics & Epidemiology	P-value and confidence interval
Subject	System	Topic

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A 28-year-old woman, gravida 3 para 2, at 31 weeks gestation comes to the office for a prenatal visit. The patient has had increasing shortness of breath while climbing stairs and during long walks for the past few weeks but has had no cough, sick contacts, hemoptysis, orthopnea, or chest pain. She has had no contractions or vaginal bleeding, and fetal movement is normal. The patient has no chronic medical conditions, and her pregnancy has been uncomplicated. Blood pressure is 110/80 mm Hg, pulse is 70/min, and respirations are 18/min. Fetal heart tones are normal. Cardiac examination reveals no rubs or murmurs. The lungs are clear to auscultation bilaterally. The remainder of the examination is unremarkable. Which of the following laboratory findings will most likely be found in this patient?

	pH	$PaCO_2$ (mm Hg)	PaO_2 (mm Hg)	Urine bicarbonate
A.	7.26	45	101	↓
B.	7.34	30	97	↑
C.	7.46	29	102	↑
D.	7.48	44	98	↓
E.	7.60	25	94	↓

Submit

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		pH	$PaCO_2$ (mm Hg)	PaO_2 (mm Hg)	Urine bicarbonate
	A. (14%)	7.26	45	101	↓
	B. (21%)	7.34	30	97	↑
✓	C. (39%)	7.46	29	102	↑
	D. (15%)	7.48	44	98	↓
	E. (8%)	7.60	25	94	↓

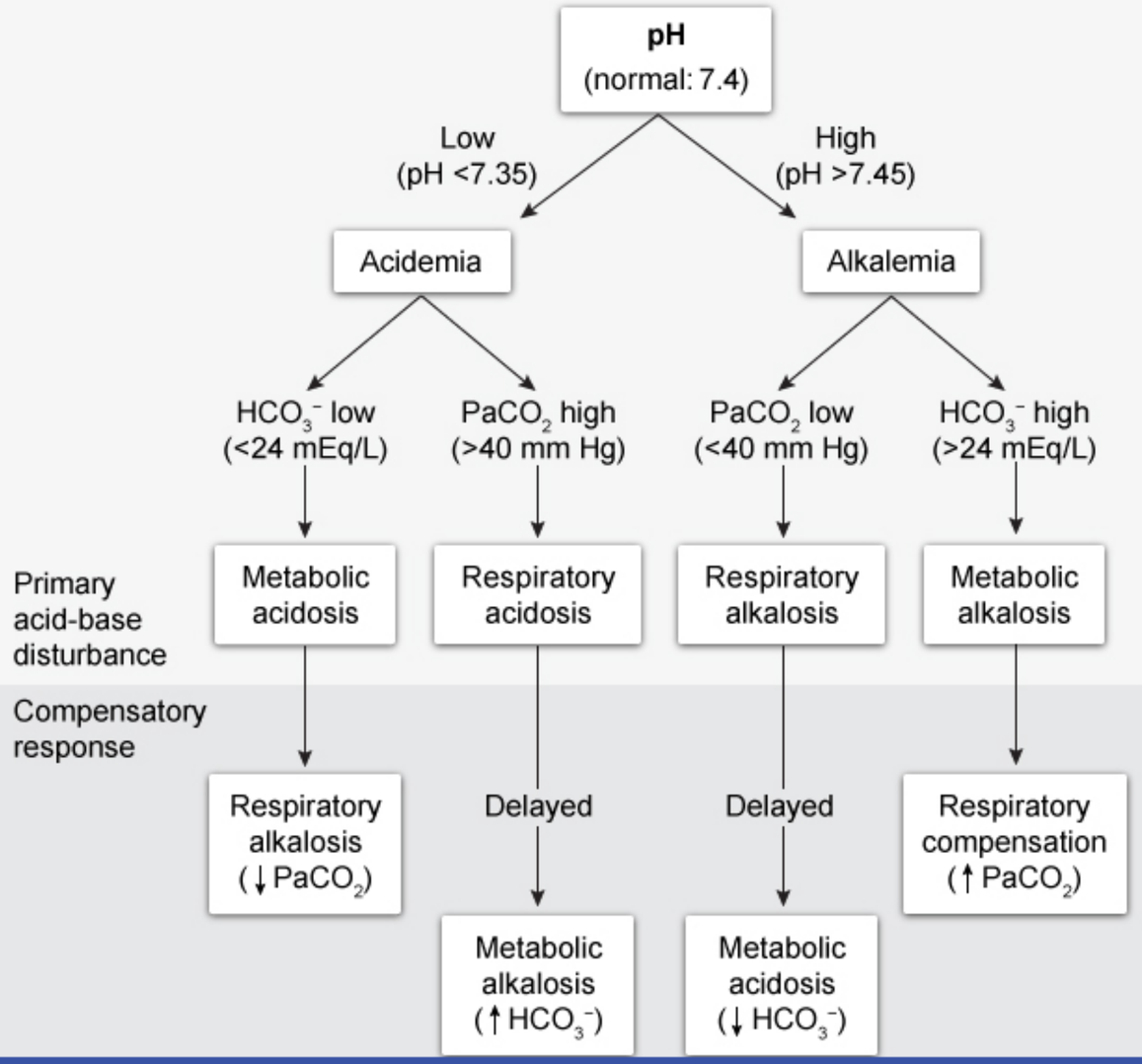
Omitted
Correct answer
C

39%
Answered correctly

02 secs
Time Spent

06/26/2020
Last Updated

Arterial blood gas interpretation of acid-base disorders



The **normal physiology of pregnancy** involves **chronic hyperventilation**. Elevated **progesterone** levels trigger a sensation of **shortness of breath** and stimulate the hypothalamus to increase respiratory drive. Ventilation is increased primarily via **increased tidal volume**, which is facilitated by increased diaphragmatic excursion and hormone-induced laxity of the intercostal muscles that allows for enlargement of the thoracic cavity (although the expanding uterus displaces the resting position of the diaphragm upward, diaphragmatic excursion is not impaired). A slight increase in respiratory rate also contributes.

The hyperventilation of pregnancy creates an expected **respiratory alkalosis** (ie, pH >7.45 and partial pressure of carbon dioxide in arterial blood [$PaCO_2$] <40 mm Hg) with metabolic compensation (**increased renal bicarbonate** [HCO_3^-] **excretion**). Arterial oxygenation is also increased slightly above normal (ie, arterial partial pressure of oxygen [PaO_2] >100 mm Hg). These changes help facilitate the transport of acidic wastes from, and the transport of oxygen to, the developing fetus.

(Choice A) Low pH (<7.35) with elevated $PaCO_2$ (>40 mm Hg) indicates respiratory acidosis. Urine HCO_3^- is low as the kidneys increase HCO_3^- reabsorption for metabolic compensation.

(Choice B) Low pH is not explained by low $PaCO_2$ (<40 mm Hg); therefore, the low $PaCO_2$ likely represents respiratory compensation for metabolic acidosis. Renal loss of HCO_3^- (ie, high urine HCO_3^-), as occurs with renal tubular acidosis, is a common cause of metabolic acidosis.

(Choice D) High pH (>7.45) is not explained by elevated $PaCO_2$; therefore, the elevated $PaCO_2$ likely represents respiratory compensation for metabolic alkalosis. Renal retention of HCO_3^- (ie, low urine HCO_3^-), as occurs with severe vomiting and diuretic overuse, commonly contributes to metabolic alkalosis.

(Choice E) High pH with low $PaCO_2$ indicates respiratory alkalosis. Urine HCO_3^- may be low in the acute setting but begins to increase after several hours to provide metabolic compensation (full metabolic compensation requires approximately 72 hours). This patient at 31 weeks gestation will have fully compensated respiratory alkalosis with increased urine HCO_3^- excretion.

Educational objective:
The normal physiology of pregnancy involves chronic hyperventilation caused by elevated progesterone levels stimulating an increase in central respiratory drive. This creates an expected respiratory alkalosis with metabolic compensation (increased renal bicarbonate excretion) that helps facilitate the transport of acidic wastes from, and the transport of oxygen to, the developing fetus.

increase in respiratory rate also contributes.

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Educational objective:
The normal physiology of pregnancy involves chronic hyperventilation caused by elevated progesterone levels stimulating an increase in central respiratory drive. This creates an expected respiratory alkalosis with metabolic compensation (increased renal bicarbonate excretion) that helps facilitate the transport of acidic wastes from, and the transport of oxygen to, the developing fetus.

Pathophysiology	Pregnancy, Childbirth & Puerperium	Respiratory alkalosis
Subject	System	Topic

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A 22-year-old woman comes to the office because of a 6-month history of increasing neck and low back pain that is most severe in the morning. Her pain improves as the day passes. The patient has no history of trauma, rashes, or urinary symptoms. Vital signs are within normal limits. Examination shows tenderness over the lumbosacral area and at the insertion site of the Achilles tendon. Forward flexion is reduced. This patient's symptoms are most likely attributable to upregulation of which of the following cytokines?

A. IL-2 and interferon gamma

B. IL-4 and interferon alpha

C. IL-5 and tumor necrosis factor-alpha

D. IL-10 and transforming growth factor-beta

E. IL-17 and tumor necrosis factor-alpha

Submit

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- A. IL-2 and interferon gamma (29%)
- B. IL-4 and interferon alpha (4%)
- C. IL-5 and tumor necrosis factor-alpha (11%)
- D. IL-10 and transforming growth factor-beta (9%)
- ✓ E. IL-17 and tumor necrosis factor-alpha (44%)

Omitted
Correct answer
E

44%
Answered correctly

02 secs
Time Spent

06/18/2020
Last Updated

Explanation

Ankylosing spondylitis	
Pathogenesis	• Altered gut biome/defective mucosal barrier • Increased production of IL-17, TNF-α & prostaglandins • Increased risk with HLA-B27

Ankylosing spondylitis	
Pathogenesis	• Altered gut biome/defective mucosal barrier • Increased production of IL-17, TNF-α & prostaglandins • Increased risk with HLA-B27

Clinical findings	• Inflammatory back & buttock pain
	  ◦ Insidious onset at age <40
	  ◦ Relieved with exercise but not rest
	  ◦ Nocturnal pain
	• Reduced chest expansion & spinal mobility
	• Enthesitis (tenderness at tendon insertion sites)
	• Dactylitis (swelling of fingers & toes)
	• Anterior uveitis

Laboratory/imaging	• Elevated ESR & CRP • Sacroiliitis: bone erosions, subchondral sclerosis, eventual bony fusion (ankylosis) • Bridging syndesmophytes: ossification at vertebral body margins (bamboo spine)

HLA-B27 = human leukocyte antigen B27; **TNF-α** = tumor necrosis factor-alpha; **CRP** = C-reactive protein; **ESR** = erythrocyte sedimentation rate.

This patient with **inflammatory back pain** (ie, age <40, insidious onset, worse with rest/better with activity) and **enthesitis** (ie, tenderness at insertion of tendons/ligaments on bone) most likely has **ankylosing spondylitis** (AS). AS is characterized by bridging syndesmophytes in the vertebral column and ankylosis (bony fusion) of the apophyseal and sacroiliac joints.

AS is an inflammatory disorder thought to **originate largely in the gut**:

- Defects in the mucosal barrier and an abnormal intestinal microbiome induce an IL-17–mediated inflammatory response via innate lymphoid cells and T helper cells (eg, Th1, Th17). The risk is greater in individuals with human leukocyte antigen B27 **(HLA-B27)**, likely due to altered

This patient with **inflammatory back pain** (ie, age <40, insidious onset, worse with rest/better with activity) and **enthesitis** (ie, tenderness at insertion of tendons/ligaments on bone) most likely has **ankylosing spondylitis** (AS). AS is characterized by bridging syndesmophytes in the vertebral column and ankylosis (bony fusion) of the apophyseal and sacroiliac joints.

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- Defects in the mucosal barrier and an abnormal intestinal microbiome induce an IL-17–mediated inflammatory response via innate lymphoid cells and T helper cells (eg, Th1, Th17). The risk is greater in individuals with human leukocyte antigen B27 **(HLA-B27)**, likely due to altered antigen presentation.
- **IL-17** stimulates production of additional inflammatory factors, primarily tumor necrosis factor-alpha (**TNF-alpha**) and **prostaglandins**, which have synergistic effects with IL-17 and induce **bony erosions** and **abnormal bone regrowth**.

Skeletal manifestations of AS occur primarily at **sites of mechanical stress**, such as the entheses, likely due to the migration of activated immune cells to these areas. Treatment options include nonsteroidal anti-inflammatory drugs (eg, ibuprofen, naproxen), which inhibit prostaglandin formation, and anti-TNF-alpha (eg, etanercept, infliximab) and anti–IL-17 (eg, secukinumab) agents.

(Choice A) IL-2 and interferon gamma have broad immune functions, including activation of the response against viruses and mycobacteria. Both cytokines inhibit Th17 cell differentiation and do not have a significant role in the pathogenesis of AS.

(Choice B) IL-4 is important in the differentiation of naïve Th cells into the Th2 subset, alternative macrophage activation (M2 type), and IgE production. It may also have a protective role in AS by limiting IL-17 production by Th1 and Th17 cells. Interferon alpha is involved primarily in antiviral activity and is not a significant factor in the pathogenesis of AS.

(Choice C) IL-5 induces B-cell growth, IgA production, and eosinophil activity. IL-5 and IL-4 are important in the etiology of certain allergic disorders (eg, allergic rhinitis, asthma), but do not contribute significantly to AS.

(Choice D) IL-10 is an antiinflammatory cytokine. Transforming growth factor-beta has antiinflammatory and profibrotic effects. These cytokines have only a minor effect in AS.

Educational objective:

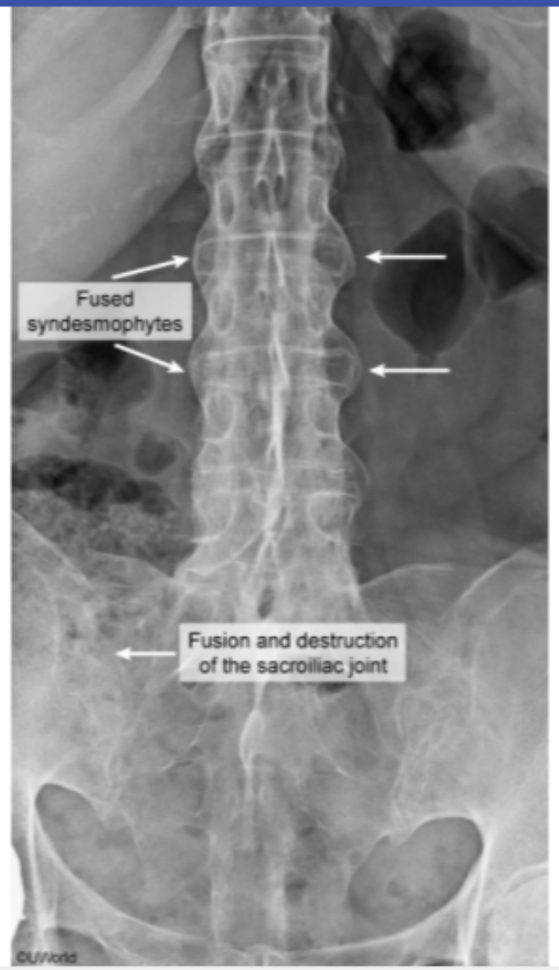
Settings

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30

Item 12 of 32
Question Id: 19493

Mark | Previous | Next | Full Screen | Tutorial | Lab Values | Notes | Calculator | Reverse Color | Text Zoom | Settings

Exhibit Display



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- **IL-17** stimulates production of additional inflammatory factors, primarily tumor necrosis factor-alpha (**TNF-alpha**) and **prostaglandins**, which have synergistic effects with IL-17 and induce **bony erosions** and **abnormal bone regrowth**.

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(Choice D) IL-10 is an antiinflammatory cytokine. Transforming growth factor-beta has antiinflammatory and profibrotic effects. These cytokines have only a minor effect in AS.

Educational objective:
The pathogenesis of ankylosing spondylitis likely originates with defects in the intestinal mucosal barrier and exposure to the gut microbiome that lead to an enhanced IL-17–mediated inflammatory response. IL-17 stimulates production of additional inflammatory factors, primarily tumor necrosis factor-alpha and prostaglandins, which have synergistic proinflammatory effects and induce bony erosions and abnormal bone regrowth in the skeleton.

Immunology	Rheumatology/Orthopedics & Sports	Ankylosing spondylitis
Subject	System	Topic

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A 24-year-old man comes to the office due to severe pain in the posterior aspect of the right foot that interferes with walking. For the last several months, the patient has also experienced a dull backache and morning stiffness that is relieved by over-the-counter ibuprofen. Family history is insignificant, and he does not use tobacco, alcohol, or illicit drugs. Which of the following is the most probable location of the pathologic process responsible for this patient's foot pain?

- A. Articular cartilage
- B. Cortical bone
- C. Periarticular bursae
- D. Synovial membrane
- E. Tendon insertion site

Submit

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A. Articular cartilage (12%)

B. Cortical bone (7%)

C. Periarticular bursae (3%)

D. Synovial membrane (12%)

✓ E. Tendon insertion site (63%)

Omitted
Correct answer
E

63%
Answered correctly

02 secs
Time Spent

06/17/2020
Last Updated

Explanation

Enthesitis	
Location of inflammation	• Sites of mechanical stress • Insertion of tendons, ligaments, joint capsules
	• Achilles tendinitis (posterior heel pain)

Enthesitis	
Location of inflammation	• Sites of mechanical stress • Insertion of tendons, ligaments, joint capsules
Common presentations	• Achilles tendinitis (posterior heel pain) • Plantar fasciitis (plantar heel pain) • Dactylitis ("sausage digits")
Disease associations	• Ankylosing spondylitis • Psoriasis/psoriatic arthritis • Reactive arthritis

This patient has inflammatory back pain (ie, onset at age <40, chronic/insidious pain and stiffness that are better with activity and worse with rest), which is likely due to **ankylosing spondylitis** (AS).

In AS, the inflammatory process is thought to originate in the gut due to an altered intestinal biome and defects in the mucosal barrier; the resulting inflammatory response leads to upregulation of cytokines (primarily tumor necrosis factor-alpha and IL-17), with activation of innate immunity and migration of immune cells to the skeleton. The resulting **skeletal manifestations** are most prominent in areas of **mechanical stress**, primarily at the **insertions of tendons**, ligaments, and joint capsules (collectively, entheses) on bone.

Enthesitis is a relatively specific finding in AS and other forms of spondyloarthritis and is characterized by local pain, tenderness, and possible swelling. Common clinical syndromes include Achilles tendinitis, plantar fasciitis, and dactylitis ("sausage digits"). **Achilles tendinitis** affects the site of insertion of the Achilles tendon on the calcaneus and typically presents with severe pain at the **posterior aspect of the heel**.

(Choices A and D) Peripheral arthritis is common in AS. In these cases, the inflammatory process largely affects the articular cartilage and subchondral bone; synovial involvement is typically minor. However, the pain is typically felt within the ankle (eg, tibiotalar and subtalar arthritis) rather than at the posterior aspect of the foot.

(Choice B) Injury to the cortical bone of the calcaneus can occur acutely due to a high-velocity fall or crush injury or chronically due to a stress

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(Choice C) Retrocalcaneal bursitis causes pain and swelling at the posterior heel near the insertion of the Achilles tendon. It is usually caused by overuse and often occurs in association with Achilles tendinopathy. However, it is significantly less common than enthesitis as a cause of posterior heel pain in AS.

Educational objective:
Enthesitis (inflammation at the bony insertions of tendons, ligaments, and joint capsules) is a prominent manifestation of spondyloarthritis (eg, ankylosing spondylitis). Common clinical syndromes include Achilles tendinitis, plantar fasciitis, and dactylitis. Achilles tendinitis affects the site of insertion of the Achilles tendon on the calcaneus and presents with severe pain at the posterior aspect of the foot.

References

- Review: enthesitis: new insights into pathogenesis, diagnostic modalities, and treatment.

migration of immune cells to the skeleton. The resulting **skeletal manifestations** are most prominent in areas of **mechanical stress**, primarily at the **insertions of tendons**, ligaments, and joint capsules (collectively, entheses) on bone.

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Pathophysiology	Rheumatology/Orthopedics & Sports	Ankylosing spondylitis
Subject	System	Topic

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A 60-year-old woman is brought to the hospital due to progressive shortness of breath and cough for 2 weeks. The patient was diagnosed with right breast cancer and completed radiation therapy 6 weeks ago. Temperature is 37.3 C (99.1 F), blood pressure is 110/70 mm Hg, pulse is 90/min, and respirations are 22/min. Oxygen saturation is 93% on room air. Examination reveals inspiratory crackles over the right lung anteriorly; the lungs are otherwise clear to auscultation. Chest radiograph shows ground-glass opacities in the right lung where radiation was delivered. Laboratory studies reveal no significant changes. Acute radiation-induced lung injury is suspected. Histopathologic examination would most likely reveal formation of which of the following?

- A. Alveolar hyaline membranes
- B. Hemosiderin-laden macrophages
- C. Necrotizing vasculitis
- D. Neutrophilic abscess

Submit

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- ✓ A. Alveolar hyaline membranes (69%)
- B. Hemosiderin-laden macrophages (9%)
- C. Necrotizing vasculitis (14%)
- D. Neutrophilic abscess (6%)

Omitted
Correct answer
A

69%
Answered correctly

01 sec
Time Spent

06/29/2020
Last Updated

Explanation

Radiation-induced lung injury usually occurs following **thoracic irradiation** for the treatment of malignancy (eg, breast or lung cancers, lymphoma). Ionizing radiation causes **DNA damage** directly (eg, double-strand breaks) and indirectly through generation of reactive oxygen and nitrogen species that can damage both DNA and other cellular components.

In the lung, this damage primarily affects the alveolar-capillary barrier, formed from alveolar epithelial cells (ie, **pneumocytes**) and vascular

Radiation-induced lung injury usually occurs following **thoracic irradiation** for the treatment of malignancy (eg, breast or lung cancers, lymphoma). Ionizing radiation causes **DNA damage** directly (eg, double-strand breaks) and indirectly through generation of reactive oxygen and nitrogen species that can damage both DNA and other cellular components.

In the lung, this damage primarily affects the alveolar-capillary barrier, formed from alveolar epithelial cells (ie, **pneumocytes**) and vascular endothelial cells, and initiates an **inflammatory response** with a cascade of cytokines (eg, IL-1, TNFα) and growth factors (eg, PDGF, TGF-β). Manifestation vary based on chronicity:

- **Acutely**, immune-mediated damage results in impaired gas exchange due to **exudative alveolitis**, with sloughing of pneumocytes and vascular endothelial cells, alveolar/interstitial edema, and **hyaline membrane formation**. Clinically, this usually manifests as dyspnea and cough 3-12 weeks after initial radiation exposure.
- **Radiation fibrosis** is a **delayed** manifestation of radiation-induced lung injury that can develop 6-12 months after initial radiation exposure. TGF-β released by immune cells and the surrounding tissue initiates fibroblast proliferation, collagen deposition, and formation of **dense fibrous bands**. The result is decreased lung volume, dilated bronchi and bronchioles (ie, traction bronchiectasis), impaired mucociliary clearance, and predisposition to **chronic infections**.

(Choices B and C) Hemosiderin-laden macrophages (due to diffuse alveolar hemorrhage) and necrotizing vasculitis are both associated with autoimmune vasculitis (eg, anti-GBM disease). These patients typically have hemoptysis and/or other systemic effects of vasculitis (eg, glomerulonephritis, arthralgias).

(Choice D) Although significant neutrophilic infiltrate occurs in patients with radiation-induced lung injury, frank formation of an abscess usually occurs following introduction of anaerobic bacteria to the lung parenchyma due to aspiration (eg, alcoholism) or septic embolism.

Educational objective:
Radiation-induced lung injury typically occurs following thoracic irradiation (eg, breast cancer), which damages pneumocytes and vascular endothelial cells and initiates an inflammatory response (eg, IL-1, TNFα, TGF-β). This immune response can have both acute (eg, exudative alveolitis, hyaline membrane formation) and delayed (eg, dense fibrosis) effects that typically manifest with cough and dyspnea.

References

- Radiation-induced lung injury (RILI).

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References

- Radiation-induced lung injury (RILI).

Pathophysiology	Pulmonary & Critical Care	Radiation injury
Subject	System	Topic

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A 32-year-old woman comes to the office due to a persistent sensation of warmth. For the last 6 months she has felt unusually warm compared to others in the room. The patient has no medical problems and takes no medications or supplements. She does not use tobacco, alcohol, or illicit drugs. Family history is significant for hypothyroidism in her mother. Temperature is 36.7 C (98 F), blood pressure is 130/60 mm Hg, and pulse is 104/min. BMI is 20 kg/m^2. On physical examination, the patient appears anxious and has a staring gaze. There is exophthalmos, lid lag, and a diffusely enlarged thyroid with an audible thyroid bruit. The patient has a fine tremor on outstretched arms, and the skin is warm and moist. Antibodies directed against which of the following are most likely to be found in this patient?

A. Thyroglobulin

B. Thyroid peroxidase

C. Thyrotropin receptor

D. Thyroxine

E. Triiodothyronine

Submit

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- A. Thyroglobulin (9%)
- B. Thyroid peroxidase (11%)
- ✓ C. Thyrotropin receptor (77%)
- D. Thyroxine (0%)
- E. Triiodothyronine (0%)

Omitted
Correct answer
C

77%
Answered correctly

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Time Spent

07/04/2020
Last Updated

Explanation

Thyroid autoantibodies	
Antibody	**Disease association**

Thyroid autoantibodies	
Antibody	**Disease association**
Thyrotropin (TSH) receptor antibody	• **Graves disease** • Functional bioassay (thyroid-stimulating immunoglobulin) is also available
Thyroid peroxidase antibody	• **Chronic lymphocytic (Hashimoto) thyroiditis** • Silent thyroiditis • Postpartum thyroiditis • Some patients with Graves disease
Thyroglobulin antibody	• Nonspecific, but more common in hypothyroidism than hyperthyroidism

This patient has signs of hyperthyroidism, including heat intolerance, tachycardia, and lid lag. In light of her diffuse goiter and exophthalmos this is very likely due to **Graves disease**. Graves disease is an autoimmune disorder triggered by **thyrotropin receptor antibodies** (TRAb), which bind and activate the TSH receptor. In addition to the thyroid, the TSH receptor antigen is present on other cell types, including fibroblasts and adipocytes. Graves ophthalmopathy is characterized by ocular irritation, impaired extraocular motion, and proptosis; it is caused by T-cell activation and stimulation of orbital fibroblasts by TRAb, leading to expansion of extraocular muscles and retro-orbital tissues.

TRAb binds to extracellular domains on the TSH receptor, a transmembrane G protein–coupled receptor. The G_s alpha subunit activates adenylate cyclase and subsequently the adenylate cyclase second messenger system. Serum TRAb immunoassays have a high sensitivity (97%) and specificity (99%) for Graves disease, although they detect both activating and blocking anti-TSH receptor antibodies. Activating antibodies can be confirmed with a functional bioassay (thyroid-stimulating immunoglobulin) that measures cyclic AMP production by a TSH-receptor–expressing cell line in response to patient serum.

(Choice A) Antibodies to thyroglobulin are thought to reflect disruption of thyroid follicles, which exposes thyroglobulin to the bloodstream. They are present in a number of autoimmune thyroid disorders but are most common in autoimmune hypothyroidism and are present in only a minority of patients with Graves disease.

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(Choice B) Thyroid peroxidase antibodies are most closely associated with Hashimoto thyroiditis and related disorders (eg, silent thyroiditis, postpartum thyroiditis). Hyperthyroidism with exophthalmos is most consistent with Graves disease.

(Choices D and E) Antibodies to thyroxine and triiodothyronine (ie, anti-T4 and anti-T3 immunoglobulins, respectively) can be detected by adding radiolabeled thyroid hormone to the patient's serum followed by precipitation of the antigen-antibody complexes with polyethylene glycol. These antibodies can be seen in a variety of autoimmune thyroid disorders, but are rare.

Educational objective:
Graves disease is an autoimmune disorder triggered by thyrotropin receptor antibodies (TRAb) that bind and activate the TSH receptor. Serum TRAb immunoassays have a high sensitivity and specificity for Graves disease.

References

- Thyrotropin receptor epitope and human leukocyte antigen in Graves disease.

Exhibit Display

Pathogenesis of Graves ophthalmopathy

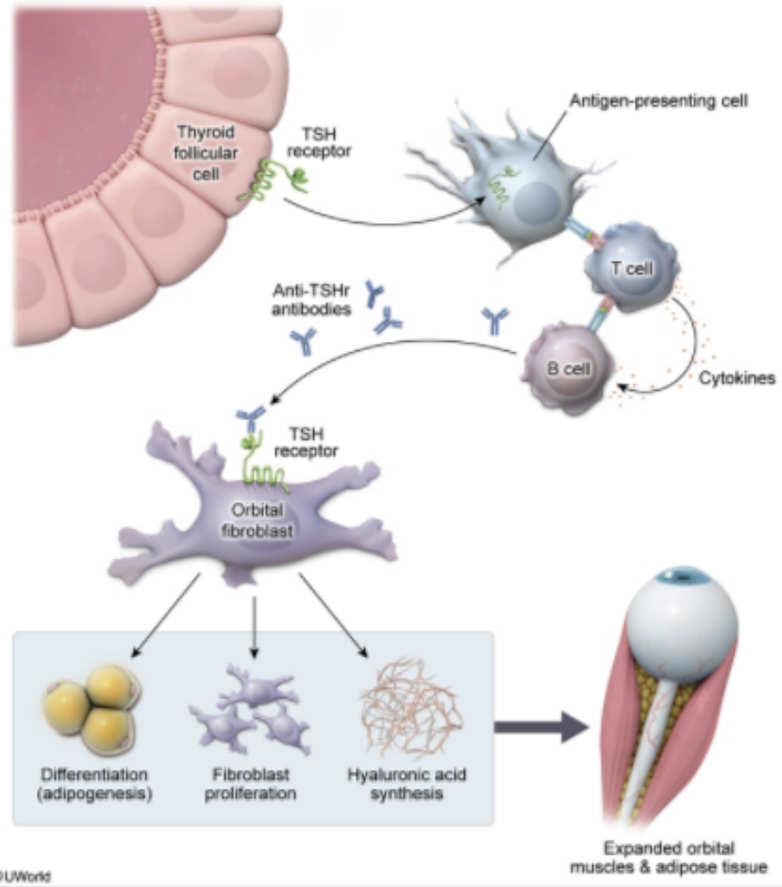

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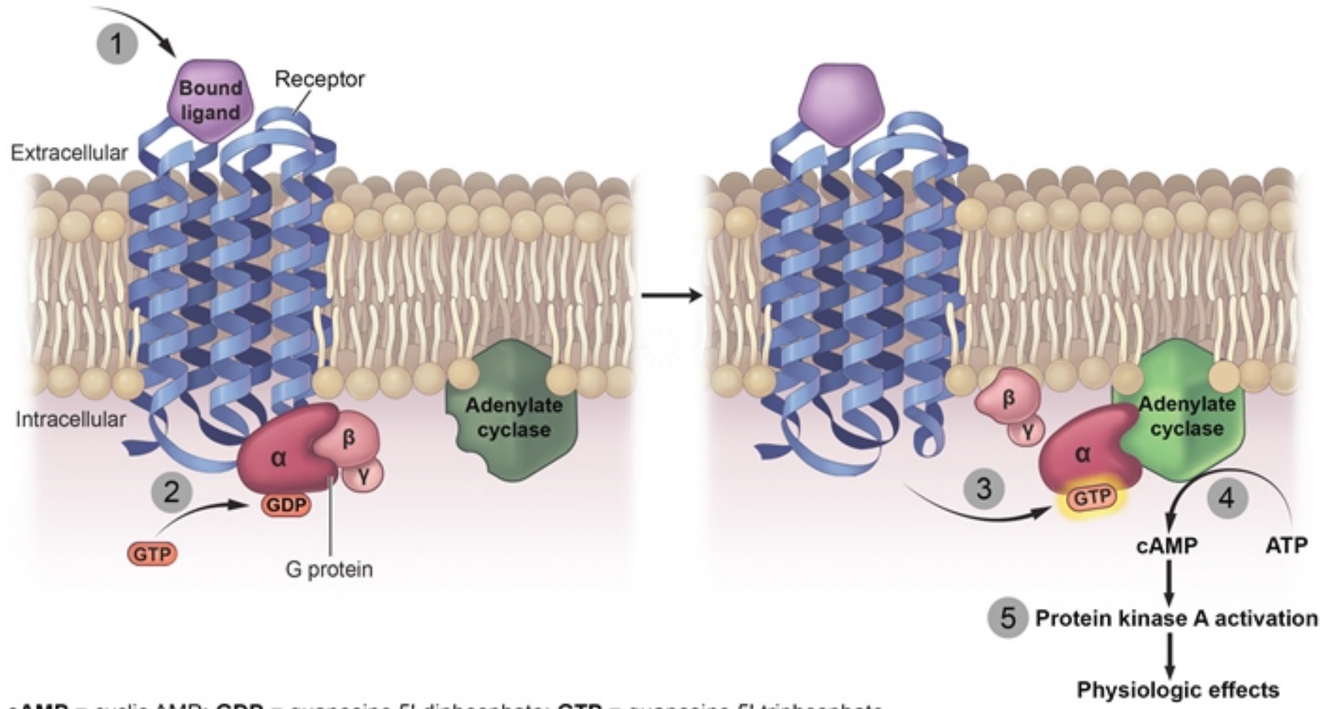
Exhibit Display

G protein activation of adenylate cyclase



cAMP = cyclic AMP; **GDP** = guanosine 5'-diphosphate; **GTP** = guanosine 5'-triphosphate.

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activation and stimulation of orbital fibroblasts by TRAb, leading to expansion of extraocular muscles and retro-orbital tissues.

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Physiology	Endocrine, Diabetes & Metabolism	Hyperthyroidism
Subject	System	Topic

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An investigator is conducting a randomized, double-blind, placebo-controlled clinical trial of a new drug for the treatment of peripheral neuropathy in adults with multiple myeloma (MM). One hundred fifty patients with MM are enrolled in the trial and randomized to receive either the new drug (n = 75) or placebo (n = 75). Trial protocol requires that patients in both groups take 1 pill per day and keep a pain diary. After 3 months of treatment, each patient is interviewed, and the pain diaries are reviewed; 9 patients taking the new drug and 3 patients taking placebo did not take the pills as instructed. The investigator decides to conduct an intention-to-treat analysis of the study data. Which of the following best describes how the data pertaining to all patients who did not adhere to protocol should be treated?

A. Conduct separate analyses of the 12 nonadherent patients and the 138 adherent patients

B. Exclude all 12 nonadherent patients from analysis

C. Exclude the 3 nonadherent patients in the group taking placebo from analysis

D. Exclude the 9 nonadherent patients in the group taking the new drug from analysis

E. Keep all 12 nonadherent patients in their respective groups for analysis

Submit

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A. Conduct separate analyses of the 12 nonadherent patients and the 138 adherent patients (12%)

B. Exclude all 12 nonadherent patients from analysis (28%)

C. Exclude the 3 nonadherent patients in the group taking placebo from analysis (1%)

D. Exclude the 9 nonadherent patients in the group taking the new drug from analysis (3%)

✓ E. Keep all 12 nonadherent patients in their respective groups for analysis (55%)

Omitted
Correct answer
E

55%
Answered correctly

02 secs
Time Spent

06/20/2020
Last Updated

Explanation

An **intention-to-treat** (ITT) analysis compares treatment groups in a randomized trial by **including all subjects** as initially allocated after randomization **regardless of what happens** during the study period. The rationale is that if subjects have such a poor treatment response (or are so inconvenienced by treatment administration or side effects) as to not follow protocol specifications or drop out of the study, then their outcomes should be attributed to that intervention (ie, nonadherence is related to the practical benefits of treatment). ITT analysis also helps avoid the

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ITT analysis may lead to a more **conservative estimate** of the effect of the intervention. If attrition or crossover is significant, ITT analysis may be less likely to identify a statistically significant difference between treatments (ie, shift toward the null hypothesis). However, results will reflect the **expected effect** of the intervention in a **practical clinical setting**.

(Choices A, C, and D) In accordance with ITT analysis, the investigator in this case should keep the 12 nonadherent patients in their respective groups for analysis.

(Choice B) An analysis that includes only those patients who strictly adhered to a research protocol (ie, excluding all nonadherent patients from analysis) follows a per-protocol (PP) principle. In PP analysis, the benefit of randomization can be lost with significant subject attrition (eg, sicker subjects selectively dropping out, introducing bias). PP analysis can also overestimate the effect of the intervention in a practical clinical setting, particularly when the treatment is somehow aversive to patients.

Educational objective:
Intention-to-treat analysis includes each subject in their initial randomization group even if subjects stop the intervention or shift to a different intervention. This approach tends to provide a conservative but more valid estimate of the intervention effect in real-world scenarios (ie, clinical settings).

Biostatistics	Biostatistics & Epidemiology	Randomized control trials
Subject	System	Topic

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Biostatistics	Biostatistics & Epidemiology	Randomized control trials
Subject	System	Topic

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A 62-year-old woman comes to the office for diarrhea. She has had 4 or 5 watery, brown stools every day for the past 6 months. Although most episodes occur during the day, she wakes up at least once a night to defecate. There is no associated hematochezia, melena, vomiting, or unexpected weight loss. Medical history is significant for type 2 diabetes mellitus and hypertension. She takes lisinopril, insulin, and metformin. She has no recent travel or new medications. Family history is unremarkable. She does not drink alcohol. Temperature is 37.4 C (99.3 F), blood pressure is 125/80 mm Hg, and pulse is 80/min. The abdomen is nontender and nondistended. Complete blood count, serum chemistries, and stool studies are normal. Which of the following is the most likely cause of this patient's diarrhea?

A. Decreased bacterial growth in the colon

B. Disaccharidase deficiency

C. Disordered motility of the small bowel and colon

D. Exocrine pancreatic insufficiency

E. Transmural intestinal inflammation

Submit

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- A. Decreased bacterial growth in the colon (7%)
- B. Disaccharidase deficiency (14%)
- ✓ C. Disordered motility of the small bowel and colon (55%)
- D. Exocrine pancreatic insufficiency (15%)
- E. Transmural intestinal inflammation (6%)

Omitted
Correct answer
C

55%
Answered correctly

02 secs
Time Spent

06/25/2020
Last Updated

Explanation

Diabetic diarrhea	
	• Long-standing hyperglycemia damages the autonomic nervous system, resulting in:

Diabetic diarrhea	
Etiology	• Long-standing hyperglycemia damages the autonomic nervous system, resulting in: ◦ Altered intestinal motility ◦ Increased intestinal secretions ◦ ± Fecal incontinence
Risk factors	• Poorly controlled diabetes mellitus • Vascular risk factors (eg, smoking, obesity, hyperlipidemia)
Manifestations	• Painless, watery diarrhea • Secretory-like (persists at night & while fasting) • Laboratory evaluation typically unremarkable

This patient with diabetes mellitus has several months of watery diarrhea that occurs both during the day and at night. In the setting of normal laboratory evaluation, this presentation suggests **diabetic diarrhea** due to **diabetic autonomic neuropathy** (DAN). Long-standing hyperglycemia results in the accumulation of cross-linked glycosylated serum proteins in the vasa nervorum, which causes inflammation and **damage to peripheral nerves**. Although this most commonly results in a distal, symmetric polyneuropathy of the feet, it can also result in damage to **sympathetic and parasympathetic nerves**, leading to autonomic dysfunction. Risk factors include poor glucose control and other vascular risk factors (eg, hypertension, obesity).

Loss of autonomic input to the gastrointestinal tract results in abnormal peristalsis, leading to **disordered small-bowel and colonic motility**, which can result in rapid intestinal transport. Furthermore, intestinal water and electrolyte secretion is increased. **Fecal incontinence** is particularly common in patients with long-standing diabetes, resulting from both a large volume of watery diarrhea and decreased anorectal sensation. Other common gastrointestinal manifestations of DAN include gastroparesis and gastroesophageal reflux.

Patients with diabetic diarrhea typically have painless, secretory-like diarrhea that **persists with fasting** (eg, nocturnal diarrhea). Laboratory evaluation, including fecal leukocytes and fecal occult blood testing, is usually unremarkable.

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(Choice A) Although altered small-bowel motility related to DAN can predispose to small intestinal bacterial overgrowth, this occurs due to an increase in small bowel bacteria, not a decrease in colonic bacterial burden. It typically causes abdominal bloating, discomfort, and gas. Nocturnal diarrhea is unexpected.

(Choice B) Lactase deficiency can cause osmotic diarrhea after lactose ingestion, leading to postprandial loose stools and bloating. However, unless patients are eating during the night, nocturnal bowel movements would not occur.

(Choice D) Exocrine pancreatic insufficiency (EPI), which is common in chronic pancreatitis or after pancreatic resection, leads to bulky, foul-smelling stool (eg, steatorrhea). Although insulin resistance can mildly impact pancreatic secretions, EPI leading to steatorrhea is rare in diabetes.

(Choice E) Crohn disease, which causes transmural gastrointestinal inflammation, can cause watery diarrhea. However, abdominal pain, anemia, abnormal stool studies (eg, fecal occult blood, fecal calprotectin), and possibly fever are expected.

Educational objective:
Prolonged hyperglycemia in diabetes mellitus can injure the parasympathetic and sympathetic nervous system, resulting in diabetic autonomic neuropathy. This can lead to disordered small-bowel and colonic motility and increased intestinal secretions, resulting in secretory-like diarrhea

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Educational objective:
Prolonged hyperglycemia in diabetes mellitus can injure the parasympathetic and sympathetic nervous system, resulting in diabetic autonomic neuropathy. This can lead to disordered small-bowel and colonic motility and increased intestinal secretions, resulting in secretory-like diarrhea (eg, fasting bowel movements).

Pathophysiology	Gastrointestinal & Nutrition	Diabetic neuropathy
Subject	System	Topic

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A 71-year-old man with a long history of smoking is found to have a new, 4-cm, irregular, spiculated, rounded mass in the right upper lobe. CT-guided biopsy is performed. Follow-up chest x-ray after the procedure is shown in the exhibit. Physical examination of the right lung would most likely show which of the following findings?

	Percussion	Tactile fremitus	Breath sounds
A.	Dullness	Decreased	Decreased
B.	Dullness	Increased	Bronchial
C.	Dullness	Increased	Decreased
D.	Hyperresonance	Decreased	Bronchial
E.	Hyperresonance	Decreased	Decreased
F.	Hyperresonance	Decreased	Increased
G.	Resonance	Normal	Vesicular

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Item 18 of 32
Question Id: 19332

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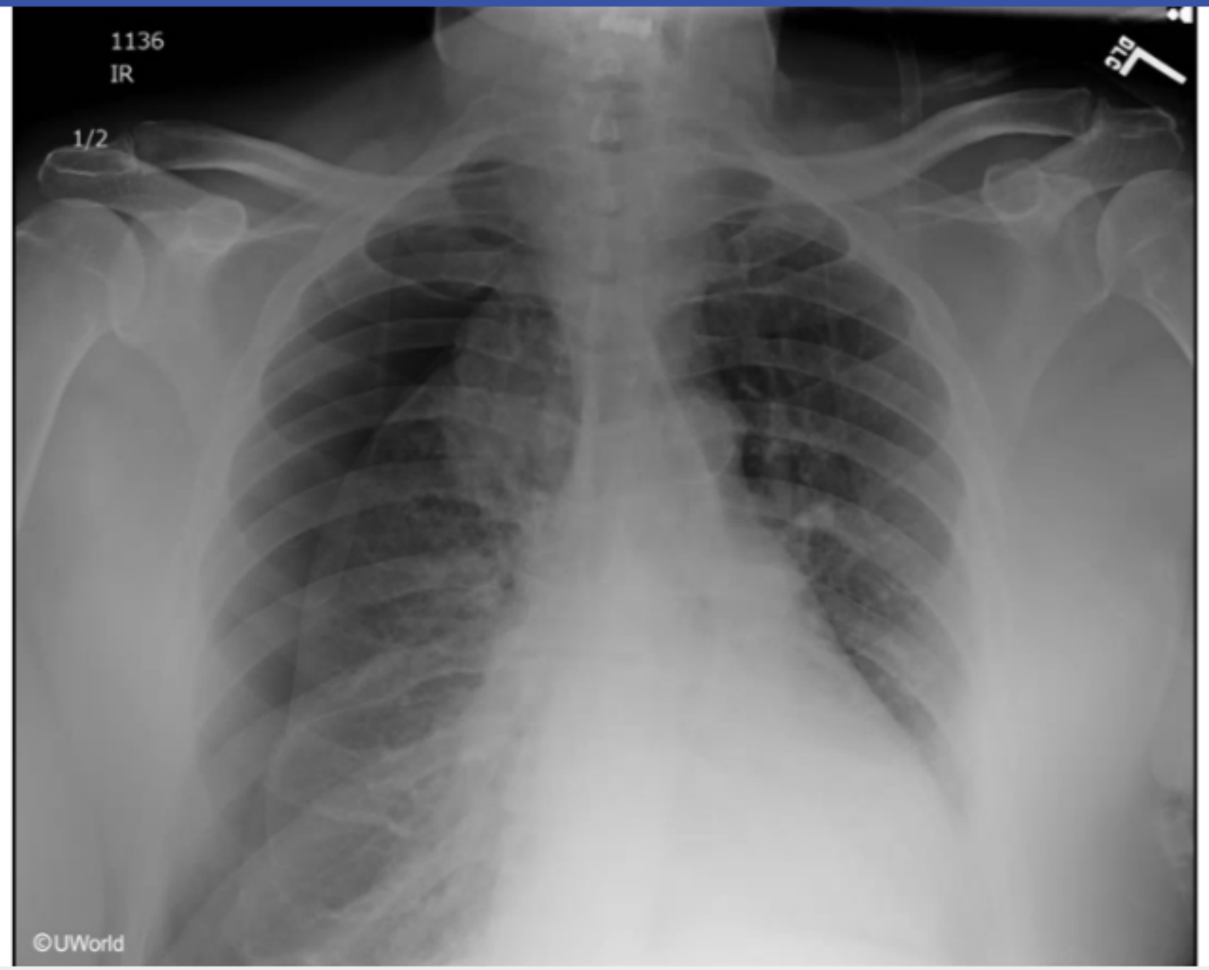

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TUTOR

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A 71-year-old man with a long history of smoking is found to have a new, 4-cm, irregular, spiculated, rounded mass in the right upper lobe. CT-guided biopsy is performed. Follow-up chest x-ray after the procedure is shown in the exhibit. Physical examination of the right lung would most likely show which of the following findings?

	Percussion	Tactile fremitus	Breath sounds
A. (14%)	Dullness	Decreased	Decreased
B. (4%)	Dullness	Increased	Bronchial
C. (8%)	Dullness	Increased	Decreased
D. (2%)	Hyperresonance	Decreased	Bronchial
✓ E. (65%)	Hyperresonance	Decreased	Decreased
F. (1%)	Hyperresonance	Decreased	Increased
G. (1%)	Resonance	Normal	Vesicular

Omitted
Correct answer
E

65%
Answered correctly

08 secs
Time Spent

06/17/2020
Last Updated

Pulmonary auscultation examination findings			
Condition	**Breath sounds**	**Tactile fremitus**	**Percussion**
Normal lung	Normal	Normal	Resonance
Consolidation	Increased	Increased	Dullness
Pleural effusion	Decreased or absent	Decreased	Dullness
Pneumothorax	Decreased or absent	Decreased	Hyperresonance
Atelectasis	Decreased or absent	Decreased	Dullness

This patient's chest x-ray after lung biopsy shows a right **pneumothorax**, which is recognized by the **continuous line** in the right lung field with **no visible lung markings** peripheral to it. This line is the outer edge of the collapsed right lung; the dark space peripheral to the lung represents air in the chest cavity.

The following characteristic physical examination findings are expected with pneumothorax:

- Tactile fremitus represents airway vibrations generated by vocalized sound (eg, saying "ninety-nine") and is measured by the examiner placing hands on the patient's back. Because air in the chest cavity insulates and dampens airway vibrations before they reach the patient's back, **decreased tactile fremitus** is expected **(Choice C)**.
- Breath sounds are caused by air movement within the airways, and the intensity varies by lung location. Vesicular breath sounds are normal over the periphery; bronchial breath sounds are higher-intensity sounds that are normal over the hilum but indicate pathology (eg, lobar consolidation) over the periphery. Because the lung is partially collapsed, leading to less air movement, and sounds from the airways are insulated by air in the chest cavity, **decreased breath sound intensity** is expected **(Choices D and F)**.
- Resonance refers to the frequency of sound generated by percussion, and it varies with density. Because air alone is less dense than a composite of lung parenchyma and air (ie, normal lung), higher-than-normal sound frequency to percussion (ie, **hyperresonance**) is expected.

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(Choice A) Like pneumothorax, fluid in the chest cavity (ie, pleural effusion) insulates airway vibrations and sounds, causing decreased tactile fremitus and breath sound intensity. However, because fluid is more dense than normal lung, dullness to percussion is expected. Atelectasis generates findings similar to those of pleural effusion; the collapsed lung reduces air movement and vibration within the airways, and the airless lung parenchyma is more dense than normal, air-filled lung.

(Choice B) Consolidated, fluid-filled lung (eg, lobar pneumonia) is more dense than normal lung. This leads to increased transmission of vibration and sound (ie, increased tactile fremitus and breath sound intensity) and dullness to percussion.

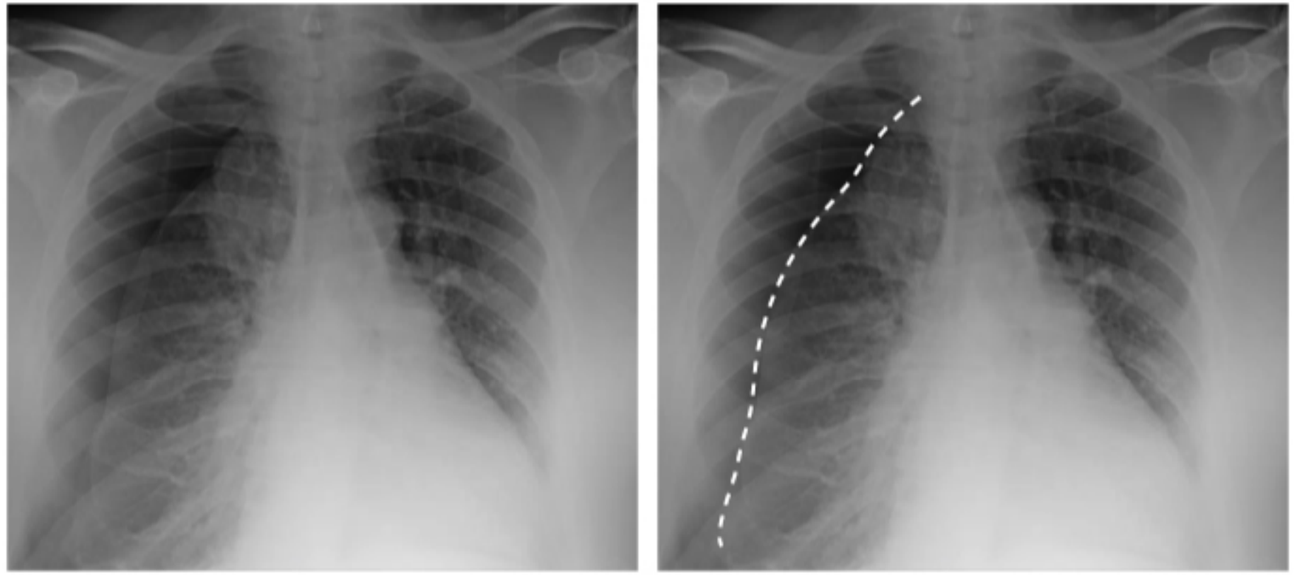
(Choice G) Normal lung demonstrates resonance to percussion, baseline tactile fremitus, and vesicular (normal-intensity) breath sounds.

Educational objective:
Pneumothorax is recognized on chest x-ray by a continuous line without lung markings peripheral to it. Decreased tactile fremitus, decreased

This patient's chest x-ray after lung biopsy shows a right **pneumothorax**, which is recognized by the **continuous line** in the right lung field with **no**

Exhibit Display

Pneumothorax



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Pneumothorax is recognized on chest x-ray by a continuous line without lung markings peripheral to it. Decreased tactile fremitus, decreased

placing hands on the patient's back. Because air in the chest cavity insulates and dampens airway vibrations before they reach the patient's back, **decreased tactile fremitus** is expected **(Choice C)**.

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(Choice G) Normal lung demonstrates resonance to percussion, baseline tactile fremitus, and vesicular (normal-intensity) breath sounds.

Educational objective:
Pneumothorax is recognized on chest x-ray by a continuous line without lung markings peripheral to it. Decreased tactile fremitus, decreased breath sound intensity, and hyperresonance to percussion are expected on physical examination.

Pathophysiology	Pulmonary & Critical Care	Pneumothorax
Subject	System	Topic

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A 67-year-old man is brought to the hospital after he developed sudden-onset altered mental status. The patient was taking care of some yardwork alongside his 17-year-old grandson during a hot summer day. The grandson does not have any symptoms. On examination, the patient's temperature is 41 C (105.8 F), blood pressure is 90/60 mm Hg, pulse is 120/min, and respirations are 24/min. Examination shows warm and dry skin. The patient is not oriented to time, place, or person. Deep tendon reflexes and muscle tone are normal. Which of the following findings in this patient most likely explains why the patient developed symptoms while his grandson remained asymptomatic?

- A. Decreased effective epidermal area available for heat transfer
- B. Decreased vasodilation of the splanchnic vasculature
- C. Increased heat transfer to the skin due to reduced subcutaneous fat
- D. Increased number of sweat glands
- E. Increased peripheral vasodilation of the skin

Submit

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- ✓ A. Decreased effective epidermal area available for heat transfer (42%)
- B. Decreased vasodilation of the splanchnic vasculature (20%)
- C. Increased heat transfer to the skin due to reduced subcutaneous fat (21%)
- D. Increased number of sweat glands (1%)
- E. Increased peripheral vasodilation of the skin (13%)

Omitted
Correct answer
A

42%
Answered correctly

02 secs
Time Spent

06/25/2020
Last Updated

Explanation

Causes of heat intolerance	
	• Deconditioning/poor physical fitness • Lack of acclimation to elevated ambient temperatures

Causes of heat intolerance	
Functional	• Deconditioning/poor physical fitness • Lack of acclimation to elevated ambient temperatures • Reduced skin surface-to-body mass ratio (eg, obesity, high muscle volume, elderly patients) • Aging-related tonic vasoconstriction of peripheral vasculature • Inherited sweat gland dysfunction
Acquired	• Drugs/medications (eg, stimulants, anticholinergics, diuretics, alcohol) • Dehydration • Large areas of scarring (eg, due to burns)

This elderly patient developed hyperthermia and altered mental status while working outside on a hot summer day. This presentation suggests exertional **heat stroke**, a life-threatening multisystem disorder characterized by **hyperthermia** (typically >40 C [104 F]) associated with **central nervous system dysfunction** (eg, encephalopathy, as seen in this disoriented patient). Other classic manifestations of heat stroke include tachycardia, tachypnea, hypotension, flushing, and end-organ dysfunction (eg, pulmonary edema, renal or hepatic failure). Diaphoresis may or may not be present on examination, depending on hydration status.

Normal thermoregulatory response to elevated temperatures include increased sweating and increased cardiac output. Furthermore, there is significant peripheral vasodilation and splanchnic vasoconstriction, which shunts blood to the periphery to aid with heat transfer. However, **elderly** patients are at particularly high risk of developing heat-related illness due to several features of normal aging that impair this response, including:

- Tonic contraction of the peripheral vasculature, which limits heat transfer to the skin
- **Reduced sweat gland density**, which limits the ability to dissipate heat via evaporation
- Loss of rete pegs and dermal capillaries, which **reduces the effective epidermal area available for heat transfer**

In addition, many elderly patients have medical conditions (eg, congestive heart failure) or are taking medications that may limit cardiac output (eg, beta blockers), diaphoresis (eg, anticholinergics), or blood volume available for heat transfer (eg, diuretics).

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In addition, many elderly patients have medical conditions (eg, congestive heart failure) or are taking medications that may limit cardiac output (eg, beta blockers), diaphoresis (eg, anticholinergics), or blood volume available for heat transfer (eg, diuretics).

(Choices B and E) Appropriate responses to elevated temperature include decreased vasodilation (ie, vasoconstriction) of the splanchnic vasculature, which promotes blood flow from the internal organs to the skin, and peripheral vasodilation, which allows for heat dissipation.

(Choice C) Loss of subcutaneous fat also often occurs with aging and reduces the ability to retain heat and allows increased heat transfer to the skin; however, this promotes cooling (and places elderly patients at increased risk for hypothermia).

(Choice D) An increased number of sweat glands would promote cooling in patients with hyperthermia; however, sweat glands are typically reduced with aging, not increased.

Educational objective:
Elderly patients are at increased risk of developing heat-related illness due to several features of normal aging that impair normal thermoregulatory mechanisms, including tonic contraction of the peripheral vasculature, reduced sweat gland density, and reduced effective epidermal area

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Pathophysiology	Poisoning & Environmental Exposure	Heat related illness
Subject	System	Topic

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A study is designed to describe the manifestations of coronavirus disease 2019 (COVID-19) on imaging studies, particularly on computerized tomography (CT) scans. Eleven patients with COVID-19 are recruited for the study, and their CT findings are studied and characterized. Which of the following best describes this study design?

A. Case-control

B. Case series

C. Clinical trial

D. Cohort

E. Cross-sectional

Submit

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- A. Case-control (4%)
- ✓ B. Case series (70%)
- C. Clinical trial (2%)
- D. Cohort (5%)
- E. Cross-sectional (16%)

Omitted
Correct answer
B

70%
Answered correctly

01 sec
Time Spent

06/20/2020
Last Updated

Explanation

Research studies are broadly classified as having an observational design or an experimental design depending on the control the researchers have over the independent variables.

- In **observational studies** (eg, case series, case-control studies, cohort studies, cross-sectional studies), the researchers have **no control** over the independent variables (eg, exposure to risk factors, treatments).
- In experimental studies (eg, crossover design, randomized controlled trials), the researchers control and randomly assign the independent variables (eg, exposure to risk factors, treatments)

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- In experimental studies (eg, crossover design, randomized controlled trials), the researchers control and randomly assign the independent variables (eg, exposure to risk factors, treatments).

Case series is a descriptive observational study design in which a (generally small) group of patients with a similar diagnosis or treatment is described at a point in time or followed over a certain time period. Contrary to other observational designs (eg, cohort, case-control), a case series has **no comparison group (Choices A and D)**. For this reason, a case series cannot establish associations between risk factors (eg, treatments) and outcomes (eg, diseases).

In this example, the CT scan findings of 11 patients with coronavirus disease 2019 (COVID-19) are being studied. The study has no control group; therefore, it can only describe COVID-19 manifestations on imaging studies.

(Choice C) A clinical trial is an experimental study in which patients are prospectively assigned to ≥2 interventions (often including a placebo or control treatment) to evaluate the effects of those interventions on outcomes of interest.

(Choice E) A cross-sectional study is an observational study that assesses a population of interest (eg, all women of reproductive age) at a single point in time; it can be used to estimate disease prevalence and association with risk factors of interest. However, it is not used to characterize disease findings because subjects are not selected based on the presence of disease.

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Biostatistics	Biostatistics & Epidemiology	Study designs
Subject	System	Topic

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A test is used to diagnose dementia in a population of 1,000 women age ≥75. The test has a sensitivity of 80% and a specificity of 90%. The test is then used as a diagnostic tool in 2 other populations of women of the same age: population 1 has a prevalence of dementia of 15%, and population 2 has a prevalence of dementia of 30%. Which of the following best describes how the negative predictive values (NPV) and the positive predictive values (PPV) from populations 1 and 2 relate to each other?

A. NPV and PPV do not change as prevalence changes

B. NPV in population 1 < NPV population 2; PPV in population 1 < PPV population 2

C. NPV in population 1 < NPV population 2; PPV in population 1 > PPV population 2

D. NPV in population 1 > NPV population 2; PPV in population 1 < PPV population 2

E. NPV in population 1 > NPV population 2; PPV in population 1 > PPV population 2

Submit

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A. NPV and PPV do not change as prevalence changes (6%)

B. NPV in population 1 < NPV population 2; PPV in population 1 < PPV population 2 (6%)

C. NPV in population 1 < NPV population 2; PPV in population 1 > PPV population 2 (6%)

✓ D. NPV in population 1 > NPV population 2; PPV in population 1 < PPV population 2 (79%)

E. NPV in population 1 > NPV population 2; PPV in population 1 > PPV population 2 (1%)

Omitted
Correct answer
D

79%
Answered correctly

02 secs
Time Spent

06/24/2020
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Explanation

Predictive values are performance measures of diagnostic tests that are **dependent on the prevalence** of disease in a population of interest.

- **Negative predictive value** (NPV) is the probability (ie, likelihood) that an individual truly does not have the disease given a negative test result. NPV is equal to the number of individuals who do not have the disease and who test negative (true negatives [TN]) divided by all those with a negative test result (TN + false negatives [FN]): **NPV** = TN / (TN + FN).
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Disease prevalence affects NPV by changing the number of TN and FN tests. It affects PPV by changing the number of TP and FP tests **(Choice A)**:

- Populations with exceptionally **low disease prevalence** (eg, prevalence close to 0%) have almost all TN (ie, more TN) with almost no TP (ie, fewer TP), and most positive tests would be FP (ie, more FP) with almost no FN (ie, fewer FN). In this scenario, NPV is close to 100%, and PPV is close to 0%. This explains why, with decreasing prevalence, **NPV increases** (more TN, fewer FN) and **PPV decreases** (fewer TP, more FP).
- Populations with exceptionally **high disease prevalence** (eg, prevalence close to 100%) have almost all TP (ie, more TP) with almost no TN (ie, fewer TN), and most negative tests would be FN (ie, more FN) with almost no FP (ie, fewer FP). In this scenario, NPV is close to 0%, and PPV is close to 100%. This explains why, with increasing prevalence, **NPV decreases** (fewer TN, more FN) and **PPV increases** (more TP, fewer FP).

(Choices B, C, and E) In this example, population 1 has a lower prevalence (15%) of dementia in women age ≥75 compared to population 2 (30%). Therefore, NPV in population 1 > NPV population 2, and PPV in population 1 < PPV population 2.

Educational objective:
Predictive values change depending on the prevalence of disease in a study population. As disease prevalence increases, the positive predictive value increases, and the negative predictive value decreases.

References

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(Choices B, C, and E) In
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Educational objective:
Predictive values change
value increases, and the r

References

Exhibit Display

Common performance measures for diagnostic tests

Parameter	Definition	Calculation
Sensitivity	The probability of a diseased person testing positive	Sensitivity = True positives / (True positives + False negatives)
Specificity	The probability of a nondiseased person testing negative	Specificity = True negatives / (True negatives + False positives)
Positive predictive value	The probability that disease is present given a positive result	PPV = True positives / (True positives + False positives)
Negative predictive value	The probability that disease is absent given a negative result	NPV = True negatives / (True negatives + False negatives)
Positive likelihood ratio	A ratio representing the likelihood of having the disease given a positive result	LR+ = Sensitivity / (1 − Specificity)
Negative likelihood ratio	A ratio representing the likelihood of having the disease given a negative result	LR− = (1 − Sensitivity) / Specificity

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PPV is equal to the number of individuals who have the disease and who test positive (true positives [TP]) divided by all those with a positive test result (TP + false positives [FP]): **PPV** = TP / (TP + FP).

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Predictive values change depending on the prevalence of disease in a study population. As disease prevalence increases, the positive predictive value increases, and the negative predictive value decreases.

References

- Diagnostic methods I: sensitivity, specificity, and other measures of accuracy.

Biostatistics	Biostatistics & Epidemiology	Sensitivity, specificity, positive predictive value PPV, negative predictive value NPV
Subject	System	Topic

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A group of researchers wants to identify factors related to hospital-acquired bacteremia caused by methicillin-resistant *Staphylococcus aureus* (MRSA). A total of 45 patients were enrolled in the study after MRSA was isolated from a blood sample taken from them on the third or subsequent day after admission. In addition, 90 patients admitted to the hospital over the same period with a length of stay >2 days who did not have bacteremia were randomly selected. The frequency of factors such as insertion of a central line or urinary catheter and surgical site infection were then compared between the 2 groups. Which of the following is the most appropriate null hypothesis for this study?

- A. Hazard ratio is equal to 1
- B. Hazard ratio is not equal to 1
- C. Odds ratio is equal to 1
- D. Odds ratio is not equal to 1
- E. Relative risk is equal to 1
- F. Relative risk is not equal to 1

Submit

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- A. Hazard ratio is equal to 1 (4%)
- B. Hazard ratio is not equal to 1 (2%)
- ✓ C. Odds ratio is equal to 1 (52%)
- D. Odds ratio is not equal to 1 (9%)
- E. Relative risk is equal to 1 (23%)
- F. Relative risk is not equal to 1 (7%)

Omitted
Correct answer
C

52%
Answered correctly

02 secs
Time Spent

06/25/2020
Last Updated

Explanation

A statistical hypothesis is an initial assumption (that may or may not be true) regarding population parameters (eg, mean values in two different groups) or the relationship between variables within a population (eg, association between an exposure and a disease). The **null hypothesis (H_0)** is a statement of no difference or **no association**. The alternative hypothesis (H_a) is a statement of difference or association.

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In this case, patients are **initially identified** based on their **disease status** (ie, cases: patients with methicillin-resistant *Staphylococcus aureus* [MRSA] bacteremia, controls: patients without MRSA bacteremia). The **frequency of factors** (ie, exposure to insertion of a central line or urinary catheter, surgical site infection) is **subsequently compared** between cases and controls. Therefore, this is a **case-control study**; the most appropriate measure of association between an exposure and a disease in case-control studies is the **odds ratio (OR)**, which represents the odds of disease among exposed patients relative to nonexposed patients.

The OR may be interpreted as follows:

- **OR = 1.0 (null value)** indicates that the odds of exposure among cases are the same as the odds of exposure among controls; therefore, **exposure is not associated with the disease**.
- OR ≠ 1.0 indicates that the odds of exposure are lower (ie, OR <1) or higher (ie, OR >1) among cases than among controls; therefore, exposure is associated with the disease.

Because H_0 is a statement of no association, the most appropriate H_0 for the study is that the OR = 1 **(Choice D)**.

(Choices A, B, E, and F) Measures of association based on risk/incidence (eg, relative risk, hazard ratio) are calculated in cohort studies and experimental designs, in which participants are initially selected based on exposure status (ie, exposed or nonexposed to a risk factor or treatment) and then are followed over time to assess development of disease. However, in case-control studies, *cases* (by definition) *already have the disease*. Therefore, case-control studies cannot calculate and compare the risk/incidence of disease between the case and control groups. Instead, case-control studies must compare the odds of exposure (to a risk modifier) between cases and controls.

Educational objective:
The odds ratio (OR) is a measure of association used in case-control studies. It quantifies the relationship between an exposure and a disease; its null value (ie, null hypothesis value) is always 1 (ie, OR = 1).

In this case, patients are **initially identified** based on their **disease status** (ie, cases: patients with methicillin-resistant *Staphylococcus aureus* [MRSA] bacteremia, controls: patients without MRSA bacteremia). The **frequency of factors** (ie, exposure to insertion of a central line or urinary catheter, surgical site infection) is **subsequently compared** between cases and controls. Therefore, this is a **case-control study**; the most appropriate measure of association between an exposure and a disease in case-control studies is the **odds ratio (OR)**, which represents the odds of disease among exposed patients relative to nonexposed patients.

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Biostatistics	Biostatistics & Epidemiology	Hypothesis testing
Subject	System	Topic

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A 46-year-old man develops episodes of "dizzy spells" accompanied by palpitations and sweating during exercise. His symptoms improve after drinking orange juice or eating a protein bar. The patient was diagnosed with type 2 diabetes 6 months ago and advised to lose weight with dietary modification and exercise. Since then, he has been working out intensively and has lost 10 kg (22 lb). Which of the following mechanisms is responsible for this patient's symptoms when exercising?

- A. Decreased hepatic glucose production
- B. Increased glucokinase activity
- C. Increased glucose-6-phosphatase activity
- D. Translocation of glucose transporter 2 to the cell membrane
- E. Translocation of glucose transporter 4 to the cell membrane

Submit

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A. Decreased hepatic glucose production (20%)

B. Increased glucokinase activity (8%)

C. Increased glucose-6-phosphatase activity (6%)

D. Translocation of glucose transporter 2 to the cell membrane (6%)

✓ E. Translocation of glucose transporter 4 to the cell membrane (58%)

Omitted
Correct answer
E

58%
Answered correctly

01 sec
Time Spent

07/01/2020
Last Updated

Explanation

Glucose uptake in skeletal muscle occurs by facilitated diffusion via **glucose transporter (GLUT) 4**. In the fed state, **insulin** induces muscular glucose uptake by stimulating translocation of GLUT4 from intracellular depots to the plasma membrane and T tubules. As circulating glucose and insulin levels fall in the fasting state, GLUT4 is resequestered, and muscle becomes increasingly dependent on internal stores of glucose and glycogen and, subsequently, on fatty acids released by lipolysis in the liver.

However, **translocation of GLUT4** is also induced by **muscle contraction**, allowing insulin-independent **glucose uptake during exercise**. Over

Glucose uptake in skeletal muscle occurs by facilitated diffusion via **glucose transporter (GLUT) 4**. In the fed state, **insulin** induces muscular glucose uptake by stimulating translocation of GLUT4 from intracellular depots to the plasma membrane and T tubules. As circulating glucose and insulin levels fall in the fasting state, GLUT4 is resequestered, and muscle becomes increasingly dependent on internal stores of glucose and glycogen and, subsequently, on fatty acids released by lipolysis in the liver.

However, **translocation of GLUT4** is also induced by **muscle contraction**, allowing insulin-independent **glucose uptake during exercise**. Over time, regular exercise also causes increased expression of GLUT4 and greater insulin-dependent GLUT4 translocation, leading to increased skeletal muscle glucose uptake at any given insulin level (ie, increased insulin sensitivity) and therefore lower blood glucose.

This patient has been engaging in a regular exercise program and is likely experiencing rapid uptake of glucose while exercising. As blood glucose levels fall, counterregulatory factors (eg, glucagon, epinephrine) are activated, leading to his symptoms (eg, palpitations, sweating), which are then relieved by the intake of sugar. **Exercise-induced hypoglycemia** is common in patients with diabetes mellitus due to the lack of physiologic insulin regulation along with insufficient carbohydrate supplementation.

(Choice A) As blood glucose levels fall during fasting or exercise, glucagon and epinephrine stimulate hepatic glycogenolysis and gluconeogenesis, leading to increased (not decreased) glucose production.

(Choice B) Glucokinase phosphorylates glucose to glucose-6-phosphate, primarily for glycogen synthesis. It is expressed mainly in the liver and is stimulated by rising, not falling, glucose levels.

(Choice C) Glucose-6-phosphatase catalyzes the hydrolysis of glucose-6-phosphate to glucose during gluconeogenesis, thereby helping to maintain glucose levels in the fasting state; increased activity would improve hypoglycemic symptoms by increasing circulating glucose levels.

(Choice D) GLUT2 is found primarily in the liver and pancreatic beta cells, where it facilitates insulin-independent glucose uptake. It is not expressed significantly in muscle or translocated in response to muscle contraction.

Educational objective:
Glucose uptake in skeletal muscle occurs primarily via glucose transporter (GLUT) 4. Muscle contraction and insulin induce translocation of GLUT4 to the cell surface, increasing glucose uptake during exercise and the fed state, respectively. Over time, regular exercise causes increased expression of GLUT4, leading to increased skeletal muscle glucose uptake at any given insulin level and therefore lower blood glucose

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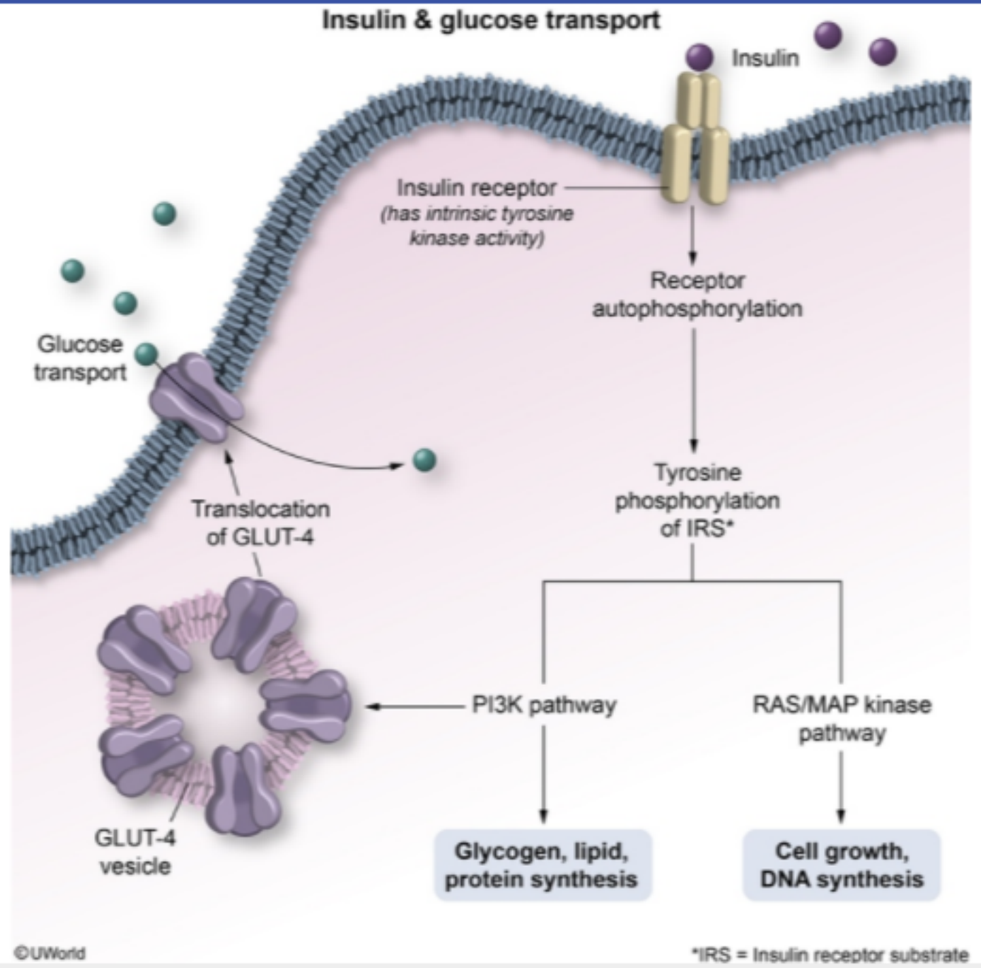

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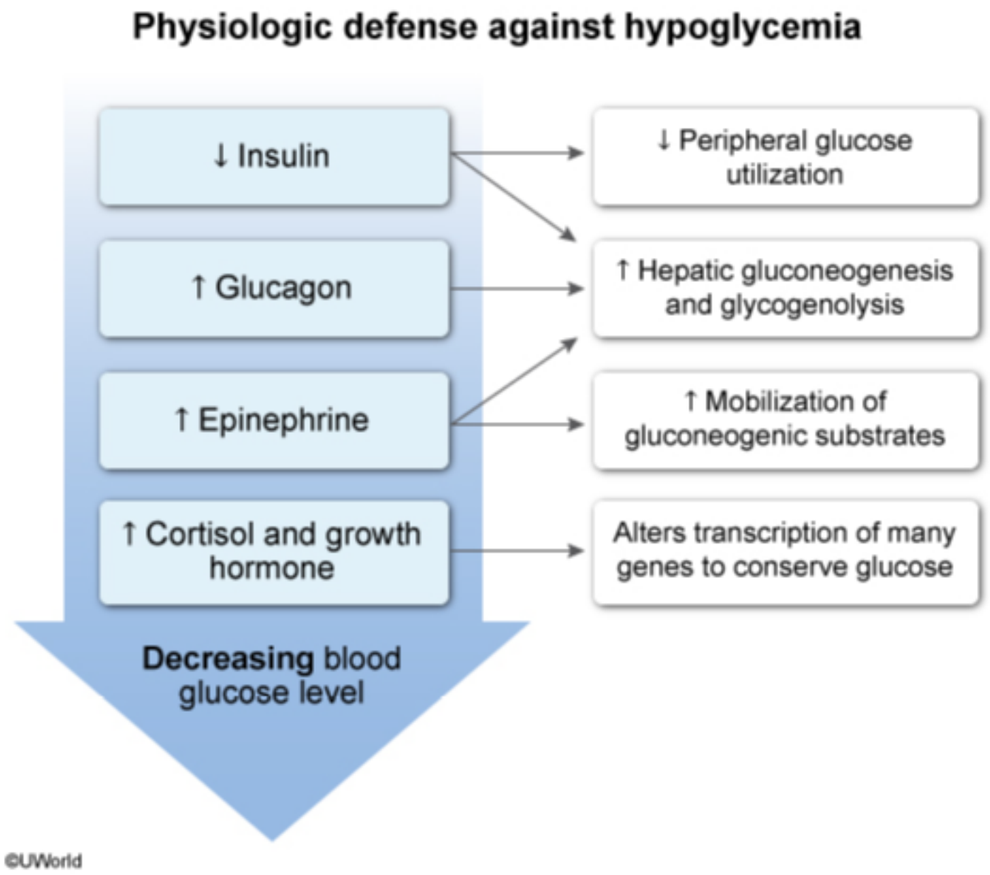

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Glucose uptake in skeletal muscle occurs primarily via glucose transporter (GLUT) 4. Muscle contraction and insulin induce translocation of GLUT4 to the cell surface, increasing glucose uptake during exercise and the fed state, respectively. Over time, regular exercise causes increased expression of GLUT4, leading to increased skeletal muscle glucose uptake at any given insulin level and therefore lower blood glucose levels.

References

- Exercise, GLUT4, and skeletal muscle glucose uptake.

Physiology	Endocrine, Diabetes & Metabolism	Diabetes mellitus
Subject	System	Topic

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A randomized controlled trial is conducted to compare transcatheter aortic valve replacement (TAVR), using a self-expanding transcatheter aortic valve bioprosthesis, with surgical aortic valve replacement in patients with severe aortic stenosis. The objective is to determine the difference in risk of death from any cause. Seven hundred forty-seven patients with severe aortic stenosis who are at increased surgical risk are recruited and randomly assigned to groups for treatment with TAVR or surgical valve replacement. Follow-up assessments are performed at discharge and at 1 month, 6 months, and 1 year. The 1-year follow-up results are as follows:

	Death from any cause		
	Yes	**No**	**Total**
TAVR	57	333	390
Surgical valve replacement	68	289	357
Total	125	622	747

Which of the following best represents the absolute risk reduction for death from any cause in patients treated with TAVR compared to those treated with surgical replacement?

A. (68/357) − (57/390) = 0.044

B. [(68/357) − (57/390)] / (68/357) = 0.233

C. (57/390) / (68/357) = 0.767

D. (68/357) / (57/390) = 1.303

E. 1 / [(68/357) − (57/390)] = 22.562

Submit

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Total	125	622	747

Which of the following best represents the absolute risk reduction for death from any cause in patients treated with TAVR compared to those treated with surgical replacement?

- A. (68/357) − (57/390) = 0.044 (68%)
- B. [(68/357) − (57/390)] / (68/357) = 0.233 (10%)
- C. (57/390) / (68/357) = 0.767 (9%)
- D. (68/357) / (57/390) = 1.303 (2%)
- E. 1 / [(68/357) − (57/390)] = 22.562 (8%)

Explanation

Absolute risk reduction (ARR) describes the difference in risk of an unfavorable outcome between the treatment group (eg, new treatment) and the control group (eg, standard treatment):

ARR = ($Risk_{control}$ − $Risk_{treatment}$)

In this example, **$Risk_{control}$** is the risk of death from any cause in the group treated with surgical aortic valve replacement and is determined by dividing the number of deaths in that group (68) by the total number of patients in that group (357). **$Risk_{treatment}$** is the risk of death from any cause in the group treated with transcatheter aortic valve replacement (TAVR) and is determined by dividing 57 by 390. Therefore, the ARR for death from any cause in patients treated with TAVR compared to those treated with surgical replacement is calculated as follows:

ARR = (68/357) − (57/390) = 0.044

ARR can be used to determine the number needed to treat (NNT), calculated as:

NNT = 1 / ARR

NNT is the number of patients who need to be treated with a treatment (eg, TAVR) to prevent 1 additional negative event (eg, death from any cause) when compared to a control group (eg, surgical replacement). A lower NNT indicates a more effective treatment because fewer patients need to be treated to prevent 1 additional negative outcome. In this example, the approximate NNT with TAVR to prevent 1 additional death from any cause is:

NNT = 1 / [(68/357) − (57/390)] = 22.562 **(Choice E)**

(Choice B) [(68/357) − (57/390)] / (68/357) = 0.233 represents the relative risk reduction (RRR) for death from any cause in the TAVR group compared to the surgical replacement group: RRR = ($Risk_{control}$ − $Risk_{treatment}$) / $Risk_{control}$. Unlike ARR, which quantifies the absolute difference in risk between the groups, RRR describes the difference in risk between the groups as a proportion of baseline risk (ie, risk in the control group).

(Choices C and D) Switching the numerator and denominator changes the interpretation of the relative risk (RR, the ratio of the probability of an event occuring in one group compared to the other group). In this example, (57/390) / (68/357) represents the RR of death from any cause in the TAVR group compared to the surgical replacement group; (68/357) / (57/390) represents the RR of death from any cause in the surgical replacement group compared to the TAVR group.

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Educational objective:

Absolute risk reduction (ARR) describes the difference in risk between control and treatment groups. It is calculated as follows: ARR = ($Risk_{control}$ − $Risk_{treatment}$).

References

- Measures of effect in epidemiological research.
- Measures of effect: relative risks, odds ratios, risk difference, and "number needed to treat."

Biostatistics	Biostatistics & Epidemiology	Risk, rate, prevalence and incidence
Subject	System	Topic

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A 16-year-old boy comes to the office for an annual health maintenance visit. He has no medical conditions and feels well. The patient plays football for his high school team and states he is planning to increase his physical workouts to prepare for the upcoming season. He indicates that last season he was often fatigued during the second half of games, and he plans to focus on endurance training. Physical examination shows no abnormalities. Which of the following is most likely to increase in this patient's large skeletal muscle groups after a prolonged period of regular training?

- A. Anaerobic glycolytic enzymes
- B. Mitochondrial content
- C. Number of motor endplates per fiber
- D. Proportion of type II (fast-twitch) fibers
- E. Total quantity of myocytes

Submit

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- A. Anaerobic glycolytic enzymes (13%)
- ✓ B. Mitochondrial content (72%)
- C. Number of motor endplates per fiber (2%)
- D. Proportion of type II (fast-twitch) fibers (7%)
- E. Total quantity of myocytes (3%)

Omitted
Correct answer
B

72%
Answered correctly

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Time Spent

07/03/2020
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Explanation

Muscle fiber characteristics		
	Type I (slow twitch)	Type II (fast twitch)
Action	Sustained force (eg, posture)	Rapid bursts (eg, heavy weightlifting)

Muscle fiber characteristics		
	Type I (slow twitch)	**Type II (fast twitch)**
Action	Sustained force (eg, posture)	Rapid bursts (eg, heavy weightlifting)
Activity type	Endurance (aerobic)	Resistance (anaerobic)
Force generated	Low	High
Resistance to fatigue	High	Low
Lipid content	High	Low
Glycogen content	Low	High
Mitochondrial content	High	Low
Energy metabolism	Oxidative	Glycolytic
Color	Red (high myoglobin)	Pale red/white (low myoglobin)
Prototype	Soleus	Triceps

Skeletal muscle fibers (or myocytes) are categorized into 2 major types based on the magnitude and sustainability of contraction force they generate and their predominant method of energy production.

Type I fibers (slow-twitch fibers) specialize in **stamina** (fatigue resistance) but can generate only relatively **low force** per contraction. These fibers primarily use **oxidative phosphorylation** (OP) to allow for sustained and efficient production of ATP. Therefore, they have a **high content** of **lipids** (fatty acids are a primary energy source for OP), **myoglobin** (to supply oxygen), and **mitochondria** (the cellular location of OP). The high myoglobin content gives these fibers a red color.

Type II fibers (fast-twitch fibers) primarily specialize in rapid bursts of strength; they generate **high force** per contraction but **quickly fatigue**. These fibers produce ATP primarily via **anaerobic glycolysis** and have **high glycogen** levels. Therefore, they have low quantities of

Prototype	Soleus	Triceps

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Targeted physical training stimulates specific phenotypic adaptations in skeletal muscle fibers to improve skeletal muscle function. **Endurance training** (eg, distance running, sustained light-to-moderate weightlifting) **promotes** the characteristics of **type I fibers** (eg, increased size and quantity of mitochondria) and also increases capillary density. In contrast, resistance training (eg, heavy weightlifting) amplifies the characteristics of type II fibers while also stimulating increased muscle mass.

(Choice A) Anaerobic glycolytic enzymes will decrease and aerobic oxidative enzymes will increase with endurance training.

(Choice C) Muscle fibers are arranged into a motor unit, with each unit innervated by a single motor neuron and endplate. Although the size and metabolic characteristics of muscle fibers change with training, the number of muscle fibers within a motor unit or endplates per fiber does not change.

(Choices D and E) Endurance training amplifies the phenotypic characteristics of existing type I fibers; however, the total quantity of muscle fibers (myocytes) or the proportion of each type of muscle fiber does not change with training.

Educational objective:
Type I muscle fibers (slow-twitch or red fibers) primarily use oxidative phosphorylation and contain high quantities of lipids, myoglobin, and mitochondria. They specialize in sustained, low force contraction, and their function is amplified by endurance training. Type II muscle fibers (fast-twitch or white fibers) primarily use glycolysis and specialize in rapid bursts of high force contraction. Their function is amplified by resistance

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Type I muscle fibers (slow-twitch or red fibers) primarily use oxidative phosphorylation and contain high quantities of lipids, myoglobin, and mitochondria. They specialize in sustained, low force contraction, and their function is amplified by endurance training. Type II muscle fibers (fast-twitch or white fibers) primarily use glycolysis and specialize in rapid bursts of high force contraction. Their function is amplified by resistance training.

References

- Exercise-induced skeletal muscle remodeling and metabolic adaptation: redox signaling and role of autophagy.

Physiology	Rheumatology/Orthopedics & Sports	Physical exercise
Subject	System	Topic

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A 35-year-old man comes to the clinic for evaluation of exertional dyspnea and dry cough for 8 months. Oxygen saturation on room air while lying down is 96% and drops to 88% after 6 minutes of walking. Examination shows fine crackles in both lower lungs. Chest x-ray reveals reticular densities in both lung fields. Lung biopsy shows an infiltration of inflammatory cells, predominantly lymphocytes, as well as poorly formed noncaseating granulomas and moderate alveolar septal fibrosis. Which of the following is the most likely diagnosis?

- A. Bronchial asthma
- B. Chronic bronchitis
- C. Hypersensitivity pneumonitis
- D. Idiopathic pulmonary fibrosis
- E. Pulmonary tuberculosis

Submit

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- A. Bronchial asthma (1%)
- B. Chronic bronchitis (3%)
- ✓ C. Hypersensitivity pneumonitis (51%)
- D. Idiopathic pulmonary fibrosis (41%)
- E. Pulmonary tuberculosis (3%)

Omitted
Correct answer
C

51%
Answered correctly

01 sec
Time Spent

07/01/2020
Last Updated

Explanation

Hypersensitivity pneumonitis	
Etiology	• Immunologic response to inhaled antigen (eg, mold, animal protein)
	Acute • Abrupt-onset fever, chills, cough, dyspnea, fatigue, leukocytosis

Hypersensitivity pneumonitis	
Etiology	• Immunologic response to inhaled antigen (eg, mold, animal protein)
Clinical presentation	**Acute** • Abrupt-onset fever, chills, cough, dyspnea, fatigue, leukocytosis • Episodes often recurrent & self-resolving **Chronic** • Progressive cough, dyspnea, fatigue, weight loss • Hypoxemia that worsens with exertion • Chest x-ray: diffuse reticular interstitial opacities (interstitial fibrosis)
Diagnosis	• PFT: restrictive pattern • BAL: high relative lymphocyte count • Lung biopsy: lymphocytic infiltrate, poorly formed noncaseating granulomas, interstitial fibrosis (chronic only)
Treatment	• Remove antigen exposure (resolves acute disease)

BAL = bronchoalveolar lavage; **PFT** = pulmonary function testing.

This patient with chronic **dyspnea and cough** accompanied by characteristic lung biopsy findings most likely has **hypersensitivity pneumonitis** (HP). HP is an exaggerated immunologic response to an inhaled antigen; common offending agents include mold, bacteria, animal protein, and chemicals. The condition has variable presentation that is largely dependent on the dose and chronicity of antigen exposure:

- **Acute HP** involves abrupt-onset and often recurring episodes of fever, chills, cough, dyspnea, and fatigue that coincide with intermittent high-dose antigen exposure. Leukocytosis is often present. Chest x-ray may be normal or show scattered micronodular opacification.
- **Chronic HP** involves persistent and **gradually progressive symptoms** (as in this patient) resulting from long-term, moderate-dose antigen exposure. Patients usually have symptoms of cough, dyspnea, fatigue, and **weight loss** for several months or more. Lung auscultation

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- **Chronic HP** involves persistent and **gradually progressive symptoms** (as in this patient) resulting from long-term, moderate-dose antigen exposure. Patients usually have symptoms of cough, dyspnea, fatigue, and **weight loss** for several months or more. Lung auscultation usually reveals **fine crackles**, and chest x-ray shows **interstitial reticular opacities** consistent with the development of pulmonary fibrosis.

The diagnosis of HP can be aided by pulmonary function testing that reveals a **restrictive pattern**; the restriction is worse with chronic HP and is accompanied by more severe impairments in gas exchange (eg, **hypoxemia**, low DLCO). Biopsy in both acute and chronic disease reveals **lymphocytic infiltrate** with poorly formed **noncaseating granulomas** created by the walling off of inhaled antigens. Chronic HP is associated with progressive **alveolar septal fibrosis**. Removal of antigen exposure usually resolves acute disease; however, the fibrosis occurring in chronic disease is often irreversible.

(Choice A) Asthma presents with intermittent cough and dyspnea. Bronchiolar biopsy can reveal noncaseating granulomas, but fibrosis is not typical and eosinophilic infiltrate is expected.

(Choice B) Chronic bronchitis presents with dyspnea and cough and is expected to cause wheezing on lung auscultation. Lymphocytic infiltrate may be present on biopsy, but granulomas are not typical.

(Choice D) Idiopathic pulmonary fibrosis can present quite similarly to chronic HP, but affected patients are usually older (eg, age >50) and granulomas are not expected on lung biopsy.

(Choice E) Pulmonary tuberculosis typically presents with fever, cough, dyspnea, night sweats, and weight loss. Lung biopsy demonstrates lymphocytic infiltrate, but caseating (rather than noncaseating) granulomas.

Educational objective:

The diagnosis of HP can be aided by pulmonary function testing that reveals a **restrictive pattern**; the restriction is worse with chronic HP and is accompanied by more severe impairments in gas exchange (eg, **hypoxemia**, low DLCO). Biopsy in both acute and chronic disease reveals **lymphocytic infiltrate** with poorly formed **noncaseating granulomas** created by the walling off of inhaled antigens. Chronic HP is associated with progressive **alveolar septal fibrosis**. Removal of antigen exposure usually resolves acute disease; however, the fibrosis occurring in chronic disease is often irreversible.

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(Choice B) Chronic bronchitis presents with dyspnea and cough and is expected to cause wheezing on lung auscultation. Lymphocytic infiltrate may be present on biopsy, but granulomas are not typical.

(Choice D) Idiopathic pulmonary fibrosis can present quite similarly to chronic HP, but affected patients are usually older (eg, age >50) and granulomas are not expected on lung biopsy.

(Choice E) Pulmonary tuberculosis typically presents with fever, cough, dyspnea, night sweats, and weight loss. Lung biopsy demonstrates lymphocytic infiltrate, but caseating (rather than noncaseating) granulomas.

Educational objective:
Hypersensitivity pneumonitis involves an exaggerated immunologic response to an inhaled antigen and can have an acute or chronic presentation. Chronic disease presents with gradually progressive cough, dyspnea, fatigue, and weight loss, and lung biopsy reveals lymphocytic infiltrate, poorly formed noncaseating granulomas, and septal fibrosis.

References

- Hypersensitivity pneumonitis.

Pathology	Pulmonary & Critical Care	Hypersensitivity pneumonitis
Subject	System	Topic

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A 24-year-old man comes to the emergency department due to worsening abdominal pain and vomiting. The patient has had 3 months of fatigue, mild abdominal pain, low-grade fever, and joint pains. On examination, the abdomen is diffusely tender to palpation with rigidity and rebound. Urgent laparotomy reveals bilateral renal infarcts and multiple segments of necrosis and perforation in the small bowel. Microscopic examination of the vessel walls shows diffuse inflammation of the adventitia and marked thickening of the inner layers due to proliferation of loose connective tissue; the arterial lumen is significantly narrowed. Which of the following is the most likely diagnosis?

- A. Bacterial endocarditis
- B. Granulomatosis with polyangiitis
- C. Inherited thrombophilia
- D. Polyarteritis nodosa
- E. Thromboangiitis obliterans

Submit

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- A. Bacterial endocarditis (0%)
- B. Granulomatosis with polyangiitis (12%)
- C. Inherited thrombophilia (1%)
- ✓ D. Polyarteritis nodosa (73%)
- E. Thromboangiitis obliterans (11%)

Omitted
Correct answer
D

73%
Answered correctly

01 sec
Time Spent

06/22/2020
Last Updated

Explanation

Polyarteritis nodosa	
Pathophysiology	• Correlation with underlying hepatitis B/C (immune complexes) • Fibrinoid necrosis of arterial wall → luminal narrowing & thrombosis → tissue ischemia

Explanation

Polyarteritis nodosa	
Pathophysiology	• Correlation with underlying hepatitis B/C (immune complexes) • Fibrinoid necrosis of arterial wall → luminal narrowing & thrombosis → tissue ischemia • Internal/external elastic lamina damage → microaneurysm formation → rupture & bleeding
Clinical features	• Constitutional: fever, weight loss, malaise • Skin: nodules, livedo reticularis, ulcers, purpura • Renal: hypertension, renal insufficiency, arterial aneurysms • Nervous: headache, seizures, mononeuritis multiplex • Gastrointestinal: mesenteric ischemia/infarction • Musculoskeletal: myalgias, arthritis
Diagnosis	• Negative ANCA & ANA • Angiography: microaneurysms & segmental/distal narrowing • Tissue biopsy: nongranulomatous transmural inflammation

ANA = antinuclear antibodies; **ANCA** = antineutrophil cytoplasmic antibodies.

This patient's systemic symptoms, renal/small-bowel infarctions, and biopsy findings are consistent with **polyarteritis nodosa** (PAN), a systemic vasculitis of **medium-sized muscular arteries**. PAN is generally marked by the following:

- Segmental, transmural inflammation of the arterial wall with invasion of neutrophils and monocytes
- Destruction of the inner portion of the arterial wall; the normal architecture is replaced with **necrotic fibrinoid material** and **loose connective tissue**, which **narrows the vessel lumen** and increases the risk of **thrombosis** and tissue infarction.
- Destruction of the internal and external elastic laminae, which increases the risk of **microaneurysms** and subsequent rupture

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- Destruction of the internal and external elastic laminae, which increases the risk of **microaneurysms** and subsequent rupture

Patients with PAN generally present with weeks or months of nonspecific **constitutional symptoms** (eg, weight loss, fatigue, low-grade fever, arthralgias) and signs of tissue ischemia in the kidneys (eg, **renal infarction**), gastrointestinal tract (eg, **small-bowel infarction**, mesenteric ischemia), peripheral nerves, and/or skin. Because PAN is **not** associated with antineutrophilic cytoplasmic antibodies or significant elevation in antinuclear antibodies, diagnostic confirmation usually requires tissue biopsy.

(Choices A and C) Bacterial endocarditis can cause embolic septic infarctions in the kidneys and intestines. Inherited coagulation disorders can also cause thrombosis with tissue infarctions. However, biopsy would show a clot/embolism in the arterial lumen (during acute infarction), not transmural inflammation and connective tissue proliferation.

(Choice B) Granulomatosis with polyangiitis usually causes manifestations in the upper/lower airways (eg, rhinosinusitis, hemoptysis) and kidneys (eg, glomerulonephritis). The gastrointestinal tract is not typically affected. Furthermore, biopsy generally reveals a leukocytoclastic vasculitis with minimal or no luminal narrowing or fibrinoid necrosis.

(Choice E) Thromboangiitis obliterans occurs primarily in young smokers. It is marked by inflammatory thrombi in the small- and medium-sized vessels of the extremities. Patients usually have digital ulcers, ischemia, gangrene, or limb claudication. Mesenteric and renal infarction would be atypical. In addition, transmural inflammation/connective tissue proliferation would not be seen during the acute stage of infarction.

Educational objective:
Polyarteritis nodosa is a systemic vasculitis of medium-sized muscular arteries marked by segmental, transmural, arterial wall inflammation with fibrinoid necrosis. This narrows the arterial lumen and increases risk of thrombosis and tissue ischemia/infarction. Damage to the internal and

- Destruction of the internal and external elastic laminae, which increases the risk of **microaneurysms** and subsequent rupture

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Educational objective:
Polyarteritis nodosa is a systemic vasculitis of medium-sized muscular arteries marked by segmental, transmural, arterial wall inflammation with fibrinoid necrosis. This narrows the arterial lumen and increases risk of thrombosis and tissue ischemia/infarction. Damage to the internal and external elastic laminae also increases the risk of microaneurysm. Tissue damage primarily occurs in the kidneys, gastrointestinal tract, neurologic system, and skin; the lungs are usually spared.

Pathology	Rheumatology/Orthopedics & Sports	Polyarteritis nodosa
Subject	System	Topic

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A 64-year-old man comes to the office for follow-up. He has a history of chronic kidney disease due to hypertensive and diabetic nephropathy. Six months ago, he developed significant fatigue and exercise intolerance. Evaluation at that time revealed normocytic anemia and normal serum iron studies so recombinant erythropoietin was initiated. Today, the patient states that his symptoms have significantly improved. Laboratory evaluation reveals a hemoglobin of 12 g/dL. If the erythropoietin treatment is continued, this patient is at greatest risk for which of the following complications?

- A. Autoimmune hemolysis
- B. Bone marrow fibrosis
- C. Gallstone formation
- D. Iron overload
- E. Venous thrombosis

Submit

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- A. Autoimmune hemolysis (1%)
- B. Bone marrow fibrosis (7%)
- C. Gallstone formation (4%)
- D. Iron overload (12%)
- ✓ E. Venous thrombosis (74%)

Omitted
Correct answer
E

74%
Answered correctly

01 sec
Time Spent

06/17/2020
Last Updated

Explanation

Erythropoietin (EPO) promotes the survival, differentiation, and proliferation of immature erythrocytes. It is produced by interstitial fibroblasts near the peritubular capillaries of the kidney in response to hypoxia; **deficiency** often occurs in the setting of chronic kidney disease due to inflammatory damage to the peritubular interstitial fibroblasts.

Patients with EPO deficiency generally present with **normocytic anemia**, low reticulocyte count, and iron studies similar to those seen in anemia

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Patients with EPO deficiency generally present with **normocytic anemia**, low reticulocyte count, and iron studies similar to those seen in anemia of chronic disease (eg, low serum iron, low/normal total iron-binding capacity). Treatment with **recombinant EPO** restores the stimulus for erythropoiesis, **increases hemoglobin**, and improves tissue oxygen delivery. However, **prolonged use** of EPO can lead to serious morbidity, including the following:

- **Thromboembolism:** EPO increases blood viscosity and triggers the release of proinflammatory cytokines from the endothelium, which increases the risk for thromboembolism. It also promotes the release of procoagulant proteins such as von Willebrand factor and plasminogen activator inhibitor-1.
- **Hypertension:** EPO increases systemic vascular resistance, possibly due to activation of erythropoietin receptors on vascular endothelial and smooth muscle cells. This can result in hypertensive encephalopathy and increased risk of **cardiovascular events** (eg, stroke, myocardial infarction).

To avoid morbidity, most studies recommend **cessation** of recombinant EPO once hemoglobin improves to **12-13 g/dL**; attempting to increase hemoglobin >13 g/dL increases the risk of adverse effects and death.

(Choice A) Autoantibodies can form against recombinant EPO, which limits its efficacy. However, recombinant EPO does not typically trigger autoantibodies against erythrocytes; therefore, hemolytic anemia would be atypical.

(Choice B) Recombinant EPO may worsen malignancy due to the promotion of vascular growth. It does not typically cause myelofibrosis or myeloproliferative disorders. However, these conditions may be triggered by the use of granulocyte colony–stimulating hormone due to excessive stimulation of granulocyte stem cells.

(Choice C) The use of recombinant EPO does not usually increase bilirubin and does not typically cause gallstones. Increased risk of gallstones can be seen with some causes of anemia such as sickle cell disease and thalassemia.

(Choice D) Recombinant EPO stimulates erythrocytosis, which can rapidly consume iron stores (it does not cause iron overload). Therefore, iron levels should be monitored before and during treatment to ensure that iron deficiency does not occur.

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(Choice D) Recombinant EPO stimulates erythrocytosis, which can rapidly consume iron stores (it does not cause iron overload). Therefore, iron levels should be monitored before and during treatment to ensure that iron deficiency does not occur.

Educational objective:
Patients with chronic kidney disease often develop normocytic anemia due to erythropoietin (EPO) deficiency. Treatment with recombinant EPO can dramatically improve tissue oxygen delivery and reduce mortality. However, prolonged or high-dose treatment can have serious side effects, most notably increased risk of hypertension and thromboembolism.

References

- Clinical use of erythropoietin in chronic kidney disease: outcomes and future prospects.

Pharmacology	Renal, Urinary Systems & Electrolytes	Erythropoietin
Subject	System	Topic

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A 36-year-old woman comes to the clinic for evaluation of a 4-month history of nonproductive cough and exertional dyspnea. Her only other medical problem is frequent heartburn, for which she takes over-the-counter antacids. Temperature is 37.1 C (98.8 F), blood pressure is 126/74 mm Hg, pulse is 88/min, and respirations are 20/min. Examination shows bilateral crackles and normal heart sounds. The remainder of the examination is unremarkable. Chest imaging shows bilateral interstitial opacities. Bronchioalveolar lavage reveals >50% of cells being lymphocytes. Which of the following is the most likely diagnosis?

- A. Asbestosis
- B. Asthma
- C. Chronic aspiration
- D. Hypersensitivity pneumonitis
- E. Pulmonary edema

Submit

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- A. Asbestosis (2%)
- B. Asthma (8%)
- C. Chronic aspiration (20%)
- ✓ D. Hypersensitivity pneumonitis (62%)
- E. Pulmonary edema (6%)

Omitted
Correct answer
D

62%
Answered correctly

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Time Spent

07/01/2020
Last Updated

Explanation

Hypersensitivity pneumonitis	
Etiology	• Immunologic response to inhaled antigen (eg, mold, animal protein)
	Acute

Hypersensitivity pneumonitis	
Etiology	• Immunologic response to inhaled antigen (eg, mold, animal protein)
Clinical presentation	**Acute** • Abrupt-onset fever, chills, cough, dyspnea, fatigue, leukocytosis • Episodes often recurrent & self-resolving **Chronic** • Progressive cough, dyspnea, fatigue, weight loss • Hypoxemia that worsens with exertion • Chest x-ray: diffuse reticular interstitial opacities (interstitial fibrosis)
Diagnosis	• PFT: restrictive pattern • BAL: high relative lymphocyte count • Lung biopsy: lymphocytic infiltrate, poorly formed noncaseating granulomas, interstitial fibrosis (chronic only)
Treatment	• Remove antigen exposure (resolves acute disease)

BAL = bronchoalveolar lavage; **PFT** = pulmonary function testing.

This patient with several months of nonproductive cough and exertional dyspnea as well as a **lymphocyte-predominant bronchoalveolar lavage** (BAL) most likely has **hypersensitivity pneumonitis** (HP). HP results from an exaggerated immunologic response that some individuals develop to an **inhaled antigen** (eg, mold, animal protein). Those most commonly affected include farmers (ie, **farmer's lung** due to exposure to moldy hay) and bird keepers (ie, **bird fancier's lung** due to exposure to avian proteins).

The presentation of HP can be acute or chronic. Acute disease usually involves recurrent episodes of abrupt-onset cough, dyspnea, fever, chills, and fatigue that correlate with intermittent antigen exposure. Chronic disease likely results from chronic, long-term antigen exposure, and presents with gradually progressive cough, dyspnea, fatigue, and weight loss over a period of several months. Lung crackles are present with both acute and chronic disease. Chest x-ray in acute disease is frequently normal, whereas **diffuse reticular interstitial opacities** are present

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The presentation of HP can be acute or chronic. Acute disease usually involves recurrent episodes of abrupt-onset cough, dyspnea, fever, chills, and fatigue that correlate with intermittent antigen exposure. Chronic disease likely results from chronic, long-term antigen exposure, and presents with gradually progressive cough, dyspnea, fatigue, and weight loss over a period of several months. Lung crackles are present with both acute and chronic disease. Chest x-ray in acute disease is frequently normal, whereas **diffuse reticular interstitial opacities** are present with **chronic disease** as a network of interstitial inflammation and **fibrosis** develops.

Normally, the leukocytes in alveolar fluid consist of approximately 85% alveolar macrophages, 10% lymphocytes, and a small percentage of neutrophils and eosinophils. With both acute and chronic HP, **BAL usually shows high relative lymphocyte count** (eg, >20%, often >50%), which helps support the diagnosis. Other causes of high relative lymphocyte count in BAL include sarcoidosis, lymphoma, and chronic fungal or mycobacterial infection.

(Choice A) Asbestosis can present with progressive dyspnea and cough, but BAL typically shows increased neutrophils and characteristic asbestos bodies.

(Choice B) Asthma is expected to cause wheezing rather than crackles on lung auscultation. BAL may show increased eosinophils as well as bronchial epithelial cells.

(Choice C) Patients with gastroesophageal reflux disease can have chronic microaspiration, leading to respiratory symptoms (eg, cough, dyspnea). However, BAL typically shows increased neutrophils and characteristic lipid-laden macrophages that result from the aspiration of lipid-containing food or drink.

(Choice E) BAL in cardiogenic pulmonary edema often demonstrates hemosiderin-laden macrophages, resulting from elevated pulmonary capillary hydrostatic pressure leading to extravasation of red blood cells into the alveoli. Leukocyte percentages are not significantly affected.

Educational objective:

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Educational objective:
Hypersensitivity pneumonitis results from an exaggerated immunologic response to an inhaled antigen (eg, mold, animal protein), and presents with cough and dyspnea of variable acuity. Bronchoalveolar lavage typically shows high relative lymphocyte count (eg, >20%), which helps support the diagnosis.

References

- An official American Thoracic Society clinical practice guideline: the clinical utility of bronchoalveolar lavage cellular analysis in interstitial lung disease.

Pathology	Pulmonary & Critical Care	Hypersensitivity pneumonitis
Subject	System	Topic

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A 28-year-old man comes to the office due to a 4-month history of pain and stiffness in the lower back and neck. Symptoms are worse with prolonged rest and in the early morning. The patient also has fatigue and poor sleep. He has no other medical conditions and takes no medications. Vital signs are normal. Examination shows limited forward bending of the trunk. Lower extremity muscle power and reflexes are normal. Which of the following is most likely to confirm the diagnosis?

- A. Complete blood count
- B. Erythrocyte sedimentation rate
- C. Nerve conduction studies
- D. Rheumatoid factor level
- E. X-ray of the pelvis

Submit

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- A. Complete blood count (1%)
- B. Erythrocyte sedimentation rate (18%)
- C. Nerve conduction studies (1%)
- D. Rheumatoid factor level (11%)
- ✓ E. X-ray of the pelvis (66%)

Omitted
Correct answer
E

66%
Answered correctly

01 sec
Time Spent

06/18/2020
Last Updated

Explanation

Ankylosing spondylitis	
Pathogenesis	• Altered gut biome/defective mucosal barrier • Increased production of IL-17, TNF-α & prostaglandins • Increased risk with HLA-B27

Ankylosing spondylitis	
Pathogenesis	• Altered gut biome/defective mucosal barrier • Increased production of IL-17, TNF-α & prostaglandins • Increased risk with HLA-B27

Clinical findings	• Inflammatory back & buttock pain
	  ◦ Insidious onset at age <40
	  ◦ Relieved with exercise but not rest
	  ◦ Nocturnal pain
	• Reduced chest expansion & spinal mobility
	• Enthesitis (tenderness at tendon insertion sites)
	• Dactylitis (swelling of fingers & toes)
	• Anterior uveitis

Laboratory/imaging	• Elevated ESR & CRP • Sacroiliitis: bone erosions, subchondral sclerosis, eventual bony fusion (ankylosis) • Bridging syndesmophytes: ossification at vertebral body margins (bamboo spine)

HLA-B27 = human leukocyte antigen B27; **TNF-α** = tumor necrosis factor-alpha; **CRP** = C-reactive protein; **ESR** = erythrocyte sedimentation rate.

This patient with **chronic pain and stiffness** in the spine and **reduced spinal mobility** likely has **ankylosing spondylitis** (AS). The pain in AS is generally better with activity and worse at night and with rest, which can lead to disrupted sleep and daytime fatigue. AS is characterized by bony erosions and excessive formation of new bone in the axial skeleton, primarily around the vertebral margins.

Patients with suspected AS should undergo x-ray of the spine and pelvis, which can assist in the diagnosis:

- **X-ray of the pelvis** shows inflammatory arthritis of the sacroiliac joints (ie, sacroiliitis), visible as joint **erosions with subchondral sclerosis**. These findings are **relatively specific** for spondylarthritis (including AS) and, in association with typical symptoms, are often

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- **Spinal x-ray** may show heterotopic ossification affecting the margins of the vertebral bodies, which are visible as **bridging syndesmophytes**. Advanced and continuous syndesmophyte formation is termed bamboo spine.

AS is a seronegative spondyloarthropathy, and there are **no serologic tests** to confirm the diagnosis. Although most cases are associated with human leukocyte antigen B27 (HLA-B27), most patients with HLA-B27 never develop AS, so this marker does not confirm the diagnosis. Patients often have elevated inflammatory markers (eg, erythrocyte sedimentation rate, C-reactive protein) and abnormal blood counts (eg, anemia, leukocytosis), but these findings are nonspecific **(Choices A and B)**.

(Choice C) Nerve conduction studies are typically used to identify peripherial nerve lesions in patients with deficits on neurologic examination. This patient has normal examination findings, so electrodiagnostics would have little utility.

(Choice D) Rheumatoid factor is used in the diagnosis of rheumatoid arthritis (RA), which typically occurs in patients age >40 and is more common in women (AS is more common in men). RA usually causes a symmetric peripheral arthritis; cervical involvement can occur, but the lumbar spine is usually spared.

Educational objective:
Ankylosing spondylitis presents with chronic back pain with reduced spinal mobility. X-rays of the spine and pelvis can aid in diagnosis by identifying specific findings such as sacroiliitis (eg, joint erosions with subchondral sclerosis and eventual ankylosis) and bridging syndesmophytes (heterotopic ossification affecting vertebral body margins).

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Pathology	Rheumatology/Orthopedics & Sports	Ankylosing spondylitis
Subject	System	Topic

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- Bridging syndesmophytes: ossification at vertebral body margins (bamboo spine)

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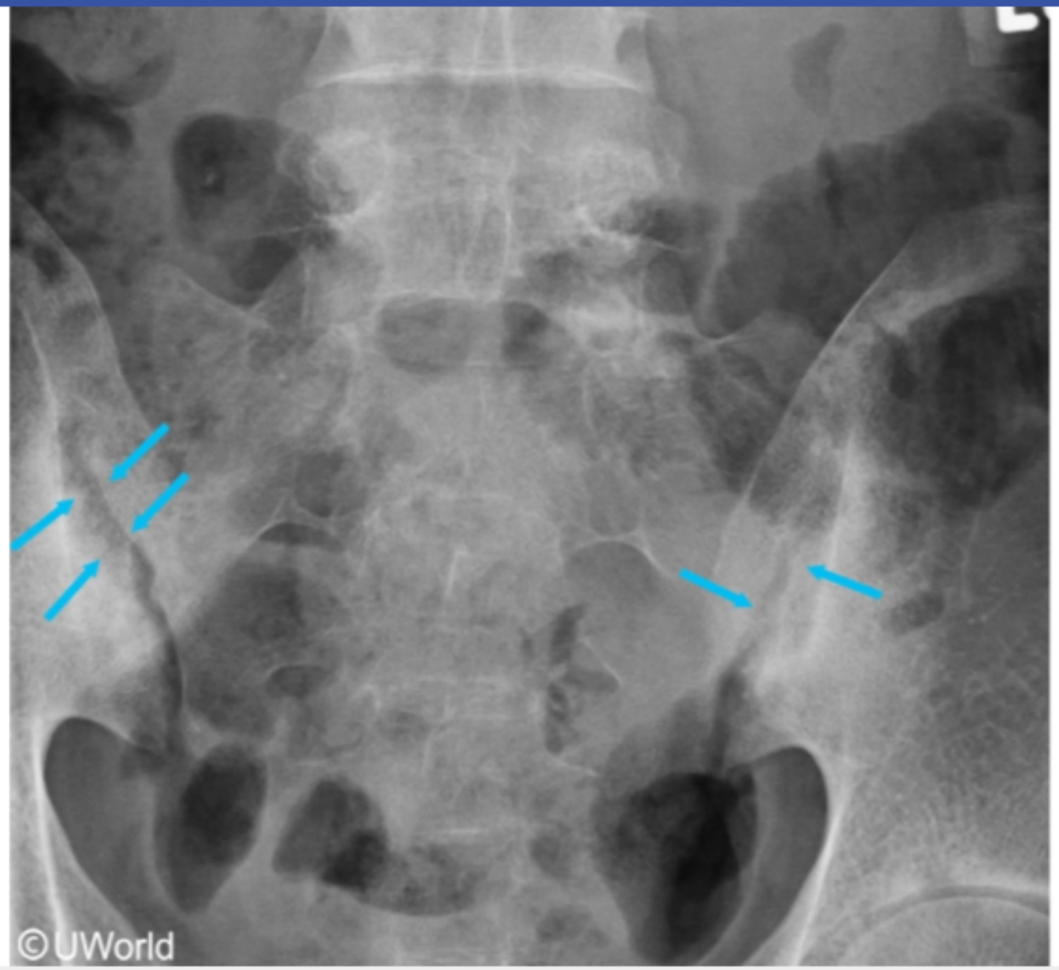

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- Bridging syndesmophytes: ossification at vertebral body margins (bamboo spine)

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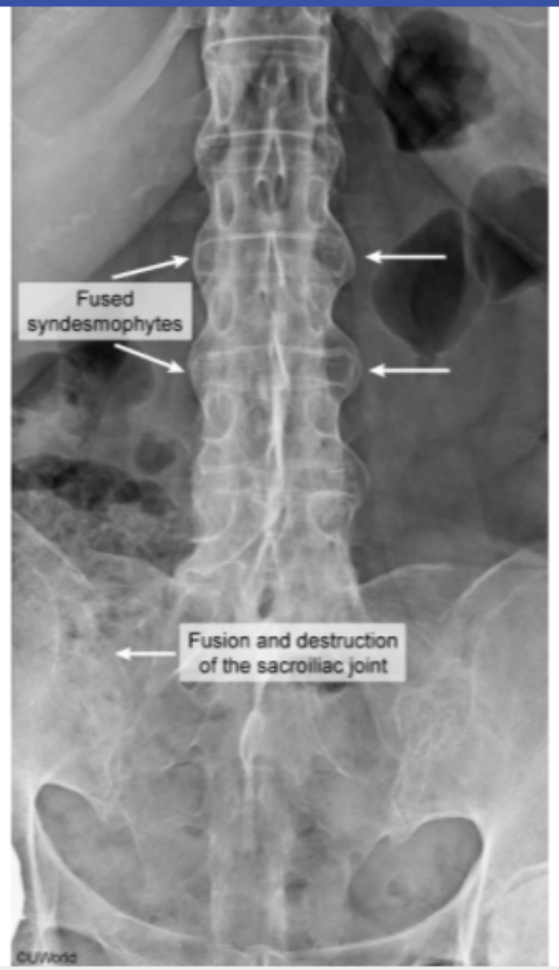

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A 64-year-old man develops diarrhea, abdominal pain, nausea, vomiting, and anorexia 3 weeks after starting radiation therapy for prostate cancer. Physical examination shows abdominal tenderness. Sigmoidoscopy reveals hyperemia, edema, erosion, and ulceration of the intestinal mucosa. Stool and serum chemistries are normal. Radiation enteritis is suspected. Which of the following is most likely the primary mechanism responsible for this patient's intestinal changes?

A. Generation of reactive oxygen species

B. Increased activity of the ubiquitin-proteasome system

C. Inhibition of DNA polymerase

D. Inhibition of thymidylate synthesis

E. Prevention of microtubule assembly

Submit

A 64-year-old man develops diarrhea, abdominal pain, nausea, vomiting, and anorexia 3 weeks after starting radiation therapy for prostate cancer. Physical examination shows abdominal tenderness. Sigmoidoscopy reveals hyperemia, edema, erosion, and ulceration of the intestinal mucosa. Stool and serum chemistries are normal. Radiation enteritis is suspected. Which of the following is most likely the primary mechanism responsible for this patient's intestinal changes?

- ✓ A. Generation of reactive oxygen species (69%)
- B. Increased activity of the ubiquitin-proteasome system (10%)
- C. Inhibition of DNA polymerase (8%)
- D. Inhibition of thymidylate synthesis (6%)
- E. Prevention of microtubule assembly (4%)

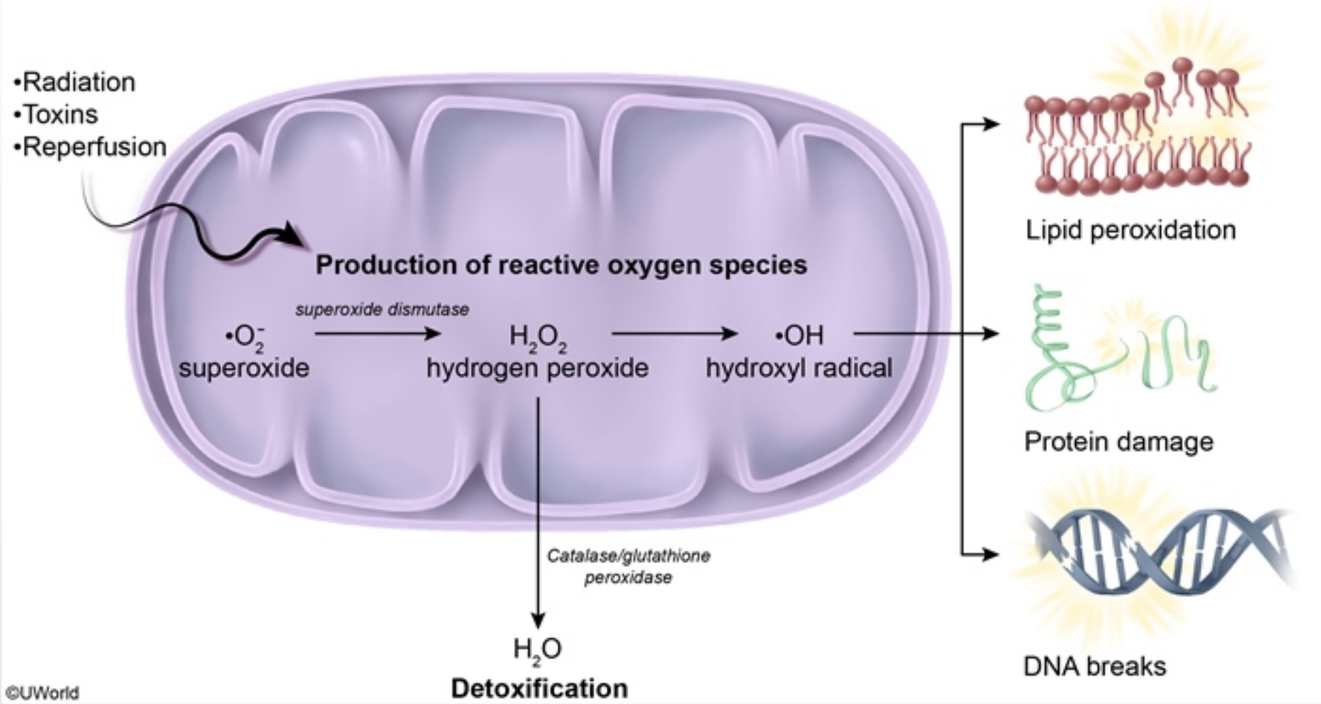
Omitted
Correct answer
A

69%
Answered correctly

02 secs
Time Spent

06/19/2020
Last Updated

Explanation



This patient developed signs of **acute radiation enteritis** (eg, abdominal pain, diarrhea, inflammation and denudation of intestinal mucosa) 3 weeks after starting radiotherapy for **prostate cancer**. Therapeutic **ionizing radiation** is commonly used to treat or palliate many types of cancer (eg, prostate, breast) and causes cell damage through 2 primary mechanisms:

- DNA double-strand breakage: Breakage of both strands is required; single-strand breaks can be repaired by polymerases.
- **Generation of reactive oxygen species**: Unstable molecules formed by the ionization of water; oxygen free radicals can cause cellular and DNA damage.

Radiation-induced DNA damage impairs mitosis and initiates **apoptosis** of susceptible cells, including **intestinal crypt stem cells** and other highly proliferative cells (eg, cancer cells, hematogenous precursors). Cellular damage also induces an immune response characterized by

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Radiation-induced DNA damage impairs mitosis and initiates **apoptosis** of susceptible cells, including **intestinal crypt stem cells** and other highly proliferative cells (eg, cancer cells, hematogenous precursors). Cellular damage also induces an immune response characterized by increased expression of **proinflammatory cytokines** (eg, IL-1, IL-6, tumor necrosis factor-alpha) and migration of leukocytes (eg, neutrophils) to the affected tissue, processes that produce additional reactive oxygen species and contribute to the radiation-induced tissue damage.

In the gastrointestinal tract, these changes result in progressive inflammation, edema, and **mucosal denudation** that decrease the absorptive area. Abdominal pain and diarrhea typically manifest several weeks after radiotherapy is started. In some cases, the effects of radiation exposure can be delayed until years after radiation exposure and present as complications of intestinal fibrosis (eg, strictures, adhesions, bowel obstruction).

(Choice B) The ubiquitin-proteasome system has an integral role in maintaining normal cell function by degrading damaged proteins and contributing to cell cycle control. Although proteasome activity normally increases in response to oxidative stress, this system is inhibited by ionizing radiation, potentiating the apoptotic effects of radiotherapy.

(Choices C, D, and E) Many chemotherapeutic agents impair essential steps in the DNA and cellular repair processes and can potentiate the effects of ionizing radiation. Although inhibition of DNA polymerase (eg, nucleoside analogues), inhibition of thymidylate synthesis (eg, 5-fluorouracil), and prevention of microtubule assembly (eg, vinblastine) would contribute to the cytotoxic effects of radiation, radiation-induced tissue damage occurs primarily through the generation of free radicals.

Educational objective:
Ionizing radiation causes cellular and DNA damage primarily through generation of reactive oxygen species, which can trigger progressive inflammation and tissue damage. In the gastrointestinal tract, the acute effects of radiation exposure typically occur several weeks after

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Ionizing radiation causes cellular and DNA damage primarily through generation of reactive oxygen species, which can trigger progressive inflammation and tissue damage. In the gastrointestinal tract, the acute effects of radiation exposure typically occur several weeks after radiotherapy is initiated and manifest as abdominal pain and diarrhea due to mucosal denudation, inflammation, and edema.

References

- Mechanisms of radiation-induced normal tissue toxicity and implications for future clinical trials

Pathology	General Principles	Radiation injury
Subject	System	Topic

A 44-year-old man comes to the office due to hand tremors. The patient first noticed the tremor 2 years ago, and it has gradually worsened. He feels well most of the time, but his hands shake uncontrollably with activities such as pouring drinks or writing notes. The symptoms are most pronounced during stressful situations such as office meetings, and he keeps his hands tightly squeezed together or hidden below the table. He has had no arm stiffness, leg symptoms, or difficulty walking, but his wife has noticed that the patient occasionally keeps nodding his head while talking. Physical examination shows obvious tremors of outstretched hands that worsen during finger-nose testing. Which of the following additional factors is most likely to be present in this patient's medical history?

A. Exacerbation with alcohol

B. Exposure to MPTP toxin

C. Family history of tremor

D. Previous head trauma

E. Use of dopaminergic drugs

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- A. Exacerbation with alcohol (8%)
- B. Exposure to MPTP toxin (12%)
- ✓ C. Family history of tremor (64%)
- D. Previous head trauma (5%)
- E. Use of dopaminergic drugs (9%)

Omitted
Correct answer
C

64%
Answered correctly

02 secs
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Explanation

Essential tremor	
Epidemiology	• Family history often present

Essential tremor	
Epidemiology	• Family history often present • Up to 5% of population affected
Clinical features	• Action tremor (eg, hands outstretched) • Usually bilateral • Hands > arms > head >> legs • Worsens with stress, improves with alcohol
Treatment	• Beta blockers: propranolol • Anticonvulsants: primidone

This patient has a worsening tremor of his distal upper extremities that becomes more pronounced with extension of his arms and at the end of an intended action (finger-to-nose test). In association with a head tremor (eg, repetitive nodding) and absence of other neurologic manifestations, this is most consistent with **essential tremor** (ET). ET is often hereditary and can be passed in an autosomal dominant fashion, so a **family history** of tremor supports the diagnosis.

Although features of ET are highly variable, it most often affects the **wrists and hands**, especially when the arms are extended. It worsens with movement (ie, **action tremor**) and improves, but may not completely abate, at rest. Although ET is not typically unilateral, it may be asymmetric. It can also affect the **head** and voice, but it generally spares the trunk and legs and is not associated with other neurologic manifestations. Although ET does not shorten life, it is slowly **progressive** and may cause patients significant social embarrassment and impair activities of daily living.

(Choice A) ET classically improves with, rather than is exacerbated by, alcohol use.

(Choices B and E) Secondary parkinsonism can be induced by MPTP (a toxic substance that destroys dopaminergic neurons in the substantia nigra) or by the use of dopamine D2 receptor blocking drugs (eg, antipsychotics, antiemetics). Patients can have tremor, but it is typically most prominent at rest and improves with action. The tremor is also accompanied by other parkinsonian features such as rigidity, postural instability,

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(Choice D) Previous head trauma can predispose to a wide range of neurologic sequelae, particularly headaches, seizures, and dementia. However, the development of isolated ET due to head trauma would be rare.

Educational objective:
Essential tremor most often presents as a tremor of the hands that is suppressed at rest, exacerbated by outstretched arms, and more pronounced during goal-directed movements. It is often hereditary (autosomal dominant) and can be associated with a head tremor, but it is not associated with other neurologic symptoms.

Pathology	Nervous System	Tremor
Subject	System	Topic

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